

## Fexofenadine Hydrochloride Tablets

» Fexofenadine Hydrochloride Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ).

**Packaging and storage**—Preserve in well-closed containers, and store at controlled room temperature.

**Labeling**—When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

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

### Identification—

**A:** *Infrared Absorption* <197K>—Weigh and finely powder a sufficient number of Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 60 mg of fexofenadine hydrochloride, to a capped tube. Add 10 mL of a mixture of acetonitrile and methanol (10 : 1), and shake or mix on a vortex mixer for 1 to 2 minutes to disperse the sample. Allow the solution to stand for 10 minutes or centrifuge for 2 to 3 minutes. Pass the liquid into a 50-mL beaker using a 0.45- $\mu$ m polytetrafluorethylene syringe filter. Evaporate the solvent until about 0.5 mL remains using a stream of nitrogen with gentle heating (do not exceed 75°). Add 5 mL of water and 5 drops of dilute hydrochloric acid, and stir to induce precipitation. Chill in an ice bath for about 30 minutes. Filter the solution through a 10- to 15- $\mu$ m sintered-glass crucible. Dry the precipitate in an air oven for 1 hour at 105°. The IR absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a potassium bromide dispersion of a similar preparation using USP Fexofenadine Hydrochloride RS. To prepare the reference standard potassium bromide dispersion, transfer about 60 mg of USP Fexofenadine Hydrochloride RS to a capped test tube and proceed as directed beginning with “Add 10 mL of a mixture of acetonitrile and methanol (10 : 1).”

**B:** 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*.

### Change to read:

#### Dissolution <711>—

TEST 1—

*Medium:* 0.001 N hydrochloric acid; 900 mL, deaerated.

*Apparatus 2:* 50 rpm.

*Times:* 10 and 30 minutes.

Determine the percentages of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved by using the following method.

*Buffer solution*—Dissolve 1.0 g of monobasic sodium phosphate, 0.5 g of sodium perchlorate, and 0.3 mL of concentrated phosphoric acid in 300 mL of water, and mix.

*Mobile phase*—Prepare a filtered and degassed mixture of acetonitrile and *Buffer solution* (7 : 3). Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).

*Standard solution*—[NOTE—A small amount of methanol, not exceeding 0.5% of the total volume, can be used to dissolve fexofenadine hydrochloride.] Dissolve an accurately weighed quantity of USP Fexofenadine Hydrochloride RS in *Medium* to obtain a solution having a known concentration similar to that expected for the solution under test.

*Resolution solution*—[NOTE—A small amount of acetic acid, not exceeding 5% of the total volume, can be used to dissolve fex-

ofenadine hydrochloride related compound A.] Dissolve an accurately weighed quantity of USP Fexofenadine Related Compound A RS in water to obtain a solution having a known concentration of about 0.44 mg per mL. Transfer 1.0 mL of this solution into a vial, add 40 mL of the *Standard solution*, and mix.

*Test solution*—Use portions of the solution under test passed through a 0.45- $\mu$ m glass fiber filter.

*Chromatographic system* (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm  $\times$  10-cm column containing packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *Resolution solution* as directed for *Procedure*: the resolution, *R*, between fexofenadine and fexofenadine related compound A is not less than 2.0. Chromatograph the *Standard solution* as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*—Separately inject equal volumes (approximately 2 to 3  $\mu$ g column load of fexofenadine hydrochloride) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the fexofenadine peaks. Calculate the quantity, in mg, of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved in the *Medium* by the formula:

$$CD(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Fexofenadine Hydrochloride RS in the *Standard solution*; *D* is the dilution factor used in preparing the *Test solution*; and *r<sub>U</sub>* and *r<sub>S</sub>* are the fexofenadine peak areas obtained from the *Test solution* and the *Standard solution*, respectively.

*Tolerances*—Not less than 60% (*Q*) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 10 minutes; and not less than 80% (*Q*) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 30 minutes.

TEST 2—If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

*Medium:* 0.001 N hydrochloric acid; 900 mL.

*Apparatus 2:* 50 rpm, use paddles and shafts coated with Teflon.

*Time:* 30 minutes.

Determine the percentage of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved by employing the following method.

*Buffer solution*—Dissolve 7.0 g of ammonium acetate in 1000 mL of water. Adjust with glacial acetic acid to a pH of  $4.0 \pm 0.05$ .

*Mobile phase*—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (3 : 2). Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).

*Standard solution 1*—Transfer about 20 mg, accurately weighed, of USP Fexofenadine Hydrochloride RS to a 100-mL volumetric flask. Add 3.0 mL of methanol, and mix. Dilute with *Medium* to volume, and mix.

*Standard solution 2*—Transfer 15.0 mL of *Standard solution 1* to a 50-mL volumetric flask, dilute with *Medium* to volume, and mix.

*Standard solution 3*—Transfer 7.5 mL of *Standard solution 1* to a 50-mL volumetric flask, dilute with *Medium* to volume, and mix.

*Test solution*—Use portions of the solution under test passed through a suitable 0.45- $\mu$ m filter.

*Chromatographic system* (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 259-nm detector and a 4.6-mm  $\times$  15-cm column that contains packing L11. The flow rate is about 1.5 mL per minute. Chromatograph any of the *Standard solutions*, and record the peak responses as directed for *Procedure*: the tailing factor is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2%.

*Procedure*—Separately inject equal volumes (30  $\mu$ L for *Standard solution 2* and 3, and 10  $\mu$ L for *Standard solution 1*) of the appro-

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appropriate *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the fexofenadine peak. Calculate the percentage of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved by the formula:

$$\frac{r_U \times C_S \times 900 \times 100}{r_S \times L}$$

in which  $r_U$  and  $r_S$  are the peak responses for the *Test solution* and the *Standard solution*,  $C_S$  is the concentration, in mg per mL, of the appropriate *Standard solution*; 900 is the volume, in mL, of *Medium*; 100 is the conversion factor to percentage; and  $L$  is the Tablet label claim, in mg.

**Tolerances**—Not less than 75% ( $Q$ ) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 30 minutes.

**TEST 3**—If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

**Medium:** 0.001 N hydrochloric acid; 900 mL for Tablets labeled to contain 30 mg or 60 mg and 1800 mL for Tablets labeled to contain 180 mg.

**Apparatus 2:** 50 rpm.

**Time:** 45 minutes.

Determine the percentage of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved by employing the following method.

**Buffer solution**—Dissolve 6.64 g of monobasic sodium phosphate monohydrate and 0.84 g of sodium perchlorate monohydrate in 1000 mL of water. Add 4 mL of triethylamine, and adjust the pH to  $2.3 \pm 0.1$  with phosphoric acid.

**Mobile phase**—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (65 : 35). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

**Stock standard solution**—Prepare a solution containing 0.5 mg per mL of USP Fexofenadine Hydrochloride RS in *Mobile phase*. This solution is stable for 3.5 months under refrigeration or for 18 days at room temperature.

**Working standard solution**—Dilute the *Stock standard solution* with *Medium* to obtain a final concentration of 0.07 mg per mL of USP Fexofenadine Hydrochloride RS. This solution is stable for 8 days under refrigeration or for 24 hours at room temperature.

**Test solution**—Pass a portion of the solution under test through a suitable 0.45- $\mu$ m filter, discarding the first 10 mL of the filtrate.

**Chromatographic system** (see *Chromatography* (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm  $\times$  10-cm column that contains 5- $\mu$ m packing L1. The flow rate is about 2.5 mL per minute. The column temperature is maintained at 40°. Chromatograph the *Working standard solution* and record the peak responses as directed for *Procedure*: the tailing factor is not more than 2.0; the theoretical plates are not less than 1000; and the relative standard deviation for replicate injections is not more than 2.0%.

**Procedure**—Separately inject equal volumes (about 20  $\mu$ L) of the *Working standard solution*, and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for fexofenadine peaks.

Calculate the percentage of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved by the formula:

$$\frac{r_U \times C_S \times V \times 100}{r_S \times L}$$

in which  $r_U$  and  $r_S$  are the peak responses for the *Test solution* and the *Working standard solution*, respectively;  $C_S$  is the concentration, in mg per mL, of the appropriate *Working standard solution*;  $V$

is the volume, in mL, of *Medium*; 100 is the conversion factor to percentage; and  $L$  is the Tablet label claim, in mg.

**Tolerances**—Not less than 75% ( $Q$ ) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 45 minutes. (RB 2-Nov-2009)

**Uniformity of dosage units** (905): meet the requirements.

**Related compounds**—

**Diluent and Mobile phase**—Prepare as directed in the Assay.

**Sensitivity solution**—Dilute 4.0 mL of the *Standard stock preparation*, prepared as directed in the Assay, with *Mobile phase* to 100 mL. Dilute 6.0 mL of this solution with *Mobile phase* to 100 mL.

**Related compound solution**—Dissolve an accurately weighed quantity of USP Fexofenadine Related Compound A RS in *Diluent*, and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.05 mg per mL.

**Standard stock solution**—Use the *Standard stock preparation*, prepared as directed in the Assay.

**Standard solution**—Dilute accurate volumes of the *Related compound solution* and the *Standard stock solution* with *Mobile phase* to obtain a solution having known concentrations of about 0.015 and 0.0045 mg per mL of fexofenadine hydrochloride and fexofenadine related compound A, respectively.

**Test stock solution**—Use the *Assay stock preparation*.

**Test solution**—Use the *Assay preparation*.

**Chromatographic system** (see *Chromatography* (621))—Proceed as directed for *Chromatographic system* under Assay. Chromatograph the *Sensitivity solution*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 6%. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 1.6 for fexofenadine related compound A, and 1.0 fexofenadine; the resolution,  $R$ , between fexofenadine and fexofenadine related compound A is not less than 7; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0% and not more than 3.0% for fexofenadine and fexofenadine related compound A, respectively.

**Procedure**—Separately inject equal volumes (about 20  $\mu$ L) of the *Standard solution*, the *Test stock solution*, and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of fexofenadine related compound A in the portion of Tablets taken by the formula:

$$100CD(r_i / r_s)/NL$$

in which  $C$  is the concentration, in mg per mL, of fexofenadine related compound A in the *Standard solution*;  $D$  is the dilution factor for the preparation of the *Test stock solution*, in mL;  $r_i$  and  $r_s$  are the peak area responses of fexofenadine related compound A in the *Test stock solution* and the *Standard solution*, respectively;  $N$  is the number of Tablets used to prepare the *Test stock solution*; and  $L$  is the label claim, in mg per Tablet, of fexofenadine hydrochloride. Calculate the percentage of the decarboxylated degradant [(±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidiny]-butyl]-isopropylbenzene; the relative retention time is 6.7] in the portion of Tablets taken by the formula:

$$100CD(r_i / r_s)/NLF$$

in which  $C$  is the concentration, in mg per mL, of USP Fexofenadine Hydrochloride RS in the *Standard solution*;  $D$  is the dilution factor for the preparation of the *Test stock solution* in mL;  $r_i$  is the peak area response of the decarboxylated degradant in the *Test stock solution*;  $r_s$  is the peak area response of fexofenadine in the *Standard solution*;  $N$  is the number of Tablets used to prepare the *Test stock solution*;  $L$  is the label claim, in mg per Tablet, of fexofenadine hydrochloride; and  $F$  is the relative response factor ( $F$  is

1.1) for the decarboxylated degradant ( $F$  is 1.0 for all other known and unknown impurities). Calculate the percentage of any other impurities in the portion of Tablets taken by the formula:

$$100r_i / (Dr_s + r_T)$$

in which  $r_i$  is the individual peak area response for an individual unknown impurity in the *Test stock solution*;  $D$  is the dilution factor, in mL, of the *Test solution*;  $r_s$  is the peak area response for fexofenadine in the *Test solution*; and  $r_T$  is the sum of the peak area responses of all unknown impurities in the *Test stock solution*: disregard any peak below 0.05%; not more than 0.4% of fexofenadine related compound A is found; not more than 0.15% of the decarboxylated degradant is found; not more than 0.2% of any individual other impurity is found; and not more than 0.5% of total impurities is found.

**Assay—**

*Acid solution*—Dilute 17 mL of glacial acetic acid with water to 1 L, and mix. Dilute 100 mL of this solution with water to 1 L.

*Buffer solution*—Dilute 15 mL of a solution containing a mixture of acetonitrile and triethylamine (1 : 1) with *Acid solution* to 1 L. Adjust with phosphoric acid to a pH of 5.25.

*Diluent*—Prepare a mixture of acetonitrile and *Acid solution* (75 : 25).

*Mobile phase*—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (64 : 36). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

*Standard stock preparation*—Dissolve an accurately weighed quantity of USP Fexofenadine Hydrochloride RS in *Diluent*, and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.25 mg per mL.

*Standard preparation*—Dilute an accurate volume of the *Standard stock preparation* with *Mobile phase* to obtain a solution having a known concentration of about 0.015 mg per mL.

*Assay stock preparation*—Transfer a sufficient number of whole Tablets (not fewer than 10) to a suitable volumetric flask, add *Acid*

*solution* (equivalent to about 20% of the total flask volume), and shake by mechanical means at a high speed for about 30 minutes or until the Tablets are fully disintegrated and finely dispersed. Add acetonitrile (equivalent to about 80% of the total flask volume), and shake by mechanical means for 60 minutes. Dilute with *Diluent* to volume, and mix. Pass a portion of this solution through a polytetrafluorethylene filter having a 0.45- $\mu$ m or finer porosity, and use the filtrate. Dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution containing about 1.2 mg of fexofenadine hydrochloride per mL.

*Assay preparation*—Dilute an aliquot of the *Assay stock preparation* quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution containing about 0.018 mg of fexofenadine hydrochloride per mL.

*Chromatographic system* (see *Chromatography* (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm  $\times$  25-cm column that contains 5- $\mu$ m packing L11. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 35°. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*—Separately inject equal volumes (about 20  $\mu$ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the fexofenadine peaks. Calculate the quantity, in mg per Tablet, of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) in the portion of Tablets taken by the formula:

$$CD(r_U / r_S)/N$$

in which  $C$  is the concentration, in mg per mL, of USP Fexofenadine Hydrochloride RS in the *Standard preparation*;  $D$  is the dilution factor used for the *Assay preparation*;  $r_U$  and  $r_S$  are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively; and  $N$  is the number of Tablets used in the *Assay preparation*.