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 (1:1), 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-µm polytetrafluorethlyene syringe filter. Evaporate the solvent until about 0.5 mL remains using a stream of nitrogen with gentle heating (do not exceed 75°C). 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-µm sintered-glass crucible. Dry the precipitate in an air oven for 1 hour at 105°C. 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 fexofenadine 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-µm glass fiber filter.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm x 15-cm column containing packing L1. The flow rate is about 1.5 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 µg column load of fexofenadine hydrochloride) of the Standard solution and the Test solution into the chromograph, 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:

\[\text{CD}(r_U / r_S)\]

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 \(r_U\) and \(r_S\) 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 pH 4.0 ± 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 2 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-µm filter.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 259-nm detector and a 4.6-mm x 15-cm column that contains packing L1. 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 µL for Standard solution 2 and 3, and 10 µL for Standard solution 1) of the appro-
Fexofenadine

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priate 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:

\[
r_1 \times C_1 \times 90(100)
\]

\[
r_2 \times L
\]

in which \( r_1 \) and \( r_2 \) are the peak responses for the Test solution and the Standard solution respectively; \( C_1 \) is the concentration, in mg per mL, of the appropriate Standard solution; \( C_2 \) 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 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 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 ± 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-µm 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 × 10-cm column that contains 5-µm 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 µL) 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 dissolved by the formula:

\[
r_1 \times C_1 \times 90(100)
\]

\[
r_2 \times L
\]

in which \( r_1 \) and \( r_2 \) are the peak responses for the Test solution and the Working standard solution, respectively; \( C_1 \) is the concentration, in mg per mL, of the appropriate Working standard solution; \( L \) is the label claim, in mg per Tablet, of fexofenadine hydrochloride; and \( F \) is the relative response factor \((F)\)

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 \( C_{32}H_{39}NO_{4} \cdot HCl \) dissolved in 45 minutes. (See 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 µL) 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:

\[100Cd(r_1/r_2)\text{/NL}\]

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; \( r_1 \) and \( r_2 \) 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 \([\text{4-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]iso- propylbenzene}; \) the relative retention time is 6.7) in the portion of Tablets taken by the formula:

\[100Cd(r_1/r_2)\text{/NLF}\]

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; \( r_1 \) is the peak area response of the decarboxylated degradant in the Test stock solution; \( r_2 \) 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 \((F)\).

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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:

\[
100r_i / (D_r S + r_T)
\]

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 stock 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-µm 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 x 25-cm column that contains 5-µm packing L1. 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 µL) 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 (C32H39NO4·HCl) in the portion of Tablets taken by the formula:

\[
CD(r_i / r_S)IN
\]

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; \( r_i \) 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.