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## Fexofenadine Hydrochloride Tablets

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<https://www.uspnf.com/rb-fexofenadine-hcl-tablets-20240426>.

### DEFINITION

Fexofenadine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ).

### IDENTIFICATION

• A. **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K

**Standard solution:** Transfer 60 mg of [USP Fexofenadine Hydrochloride RS](#) to a suitable capped tube and add 10 mL of a mixture of [acetonitrile](#) and [methanol](#) (10:1).

**Sample solution:** Transfer an equivalent to 60 mg of fexofenadine hydrochloride, from a sufficient number of weighed and finely powdered Tablets, to a suitable capped tube, and add 10 mL of a mixture of [acetonitrile](#) and [methanol](#) (10:1).

**Analysis:** Shake or mix the *Standard solution* and *Sample solution* on a vortex mixer for 1–2 min to disperse the sample. Allow the solution to stand for 10 min, or centrifuge for 2–3 min. Pass the liquid into a 50-mL beaker using a 0.45- $\mu$ m polytetrafluoroethylene 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 30 min. Filter the solution through a 10- to 15- $\mu$ m sintered-glass crucible. Dry the precipitate in an air oven for 1 h at 105° oven for 1 h at 105°. Prepare a bromide dispersion from the residue.

**Acceptance criteria:** The IR absorption spectrum of the potassium bromide dispersion of the residue from the sample exhibits maxima only at the same wavelengths as that of a potassium bromide dispersion from the Standard.

• B. The retention time of the major peak in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

### ASSAY

• PROCEDURE

**Solution A:** [Glacial acetic acid](#) and [water](#) (17:983). Dilute 100 mL of this solution with [water](#) to 1 L.

**Solution B:** Dilute 15 mL of a solution containing [acetonitrile](#) and [triethylamine](#) (1:1) with *Solution A* to 1 L. Adjust with [phosphoric acid](#) to a pH of 5.25.

**Diluent:** [Acetonitrile](#) and *Solution A* (3:1)

**Mobile phase:** [Acetonitrile](#) and *Solution B* (9:16)

**Standard stock solution:** 0.25 mg/mL of [USP Fexofenadine Hydrochloride RS](#) in *Diluent*

**Standard solution:** 0.015 mg/mL from the *Standard stock solution* in *Mobile phase*

**Sample stock solution:** Transfer a sufficient number of whole Tablets (NLT 10) to a suitable volumetric flask, add *Solution A* (equivalent to 20% of the total flask volume), and shake by mechanical means at a high speed for 30 min or until the Tablets are fully disintegrated and finely dispersed. Add [acetonitrile](#) (sufficient to fill the flask to 80% of its volume), and shake by mechanical means for 60 min. Dilute with *Diluent* to volume. Pass a portion of this solution through a polytetrafluoroethylene filter having a 0.45- $\mu$ m or finer pore size, and use the filtrate. Dilute, if necessary, with *Diluent* to obtain a solution containing an equivalent to 1.2 mg/mL of fexofenadine hydrochloride.

**Sample solution:** 0.018 mg/mL from the *Sample stock solution* in *Mobile phase*

### Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 25-cm; 5- $\mu$ m packing [L11](#)

**Column temperature:** 35°

**Flow rate:** 1.5 mL/min

**Injection volume:** 20  $\mu$ L

### 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  $C_{32}H_{39}NO_4 \cdot HCl$  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 Fexofenadine Hydrochloride RS](#) in the Standard solution (mg/mL)

$C_U$  = nominal concentration of fexofenadine hydrochloride in the Sample solution (mg/mL)

**Acceptance criteria:** 93.0%–107.0%

**PERFORMANCE TESTS**• [Dissolution \(711\)](#)**Test 1**

**Medium:** 0.001 N [hydrochloric acid](#); 900 mL, deaerated

**Apparatus 2:** 50 rpm

**Time:** 10 and 30 min

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

**Solution A:** 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](#)

**Mobile phase:** [Acetonitrile](#) and Solution A (7:3)

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

**System suitability solution:** 0.44 mg/mL of [USP Fexofenadine Related Compound A RS](#) in [water](#). Transfer 1.0 mL of this solution into a vial, and add 40 mL of the Standard solution. [NOTE—A small amount of [glacial acetic acid](#), not exceeding 5% of the total volume, can be used to dissolve fexofenadine related compound A.]

**Sample solution:** Pass portions of the solution under test through a glass fiber filter having a 0.45- $\mu$ m pore size.

**Chromatographic system**

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm  $\times$  10-cm; packing [L1](#)

**Flow rate:** 1 mL/min

**Injection volume:** 2–3  $\mu$ g column load of fexofenadine hydrochloride

**System suitability**

**Samples:** Standard solution and System suitability solution

**Suitability requirements**

**Resolution:** NLT 2.0 between fexofenadine and fexofenadine related compound A, System suitability solution

**Relative standard deviation:** NMT 2.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of  $C_{32}H_{39}NO_4 \cdot HCl$  dissolved in the portion of Tablets taken:

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

$r_U$  = peak area from the Sample solution

$r_S$  = peak area from the Standard solution

$C_S$  = concentration of [USP Fexofenadine Hydrochloride RS](#) in the Standard solution (mg/mL)

$L$  = Tablet label claim (mg)

$D$  = dilution factor of the Sample solution

$V$  = volume of Medium, 900 mL

**Tolerances:** NLT 60% (Q) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 10 min; NLT 80% (Q) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved in 30 min.

**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 min

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

**Solution A:** 7 mg/mL of [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of  $4.0 \pm 0.05$ .

**Mobile phase:** [Acetonitrile](#) and [Solution A](#) (2:3)

**Standard solution 1:** Transfer 20 mg of [USP Fexofenadine Hydrochloride RS](#) to a 100-mL volumetric flask. Add 3.0 mL of [methanol](#), and mix. Dilute with [Medium](#) to volume.

**Standard solution 2:** Transfer 15.0 mL of *Standard solution 1* to a 50-mL volumetric flask. Dilute with [Medium](#) to volume.

**Standard solution 3:** Transfer 7.5 mL of *Standard solution 1* to a 50-mL volumetric flask. Dilute with [Medium](#) to volume.

**Sample solution:** Pass portions of the solution under test through a suitable filter of 0.45- $\mu$ m pore size.

#### Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 259 nm

**Column:** 4.6-mm  $\times$  15-cm; packing [L11](#)

**Flow rate:** 1.5 mL/min

**Injection volume:** 10  $\mu$ L for *Standard solution 1* and 30  $\mu$ L for *Standard solutions 2* and *3*

#### System suitability

**Sample:** Any of the *Standard solutions*

#### Suitability requirements

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

#### Analysis

**Samples:** *Standard solutions 1, 2, and 3* and the *Sample solution*

Calculate the percentage of  $C_{32}H_{39}NO_4 \cdot HCl$  dissolved in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times (C_s/L) \times V \times 100$$

$r_u$  = peak area from the *Sample solution*

$r_s$  = peak area from the *Standard solution*

$C_s$  = concentration of the appropriate *Standard solution* (mg/mL)

$V$  = volume of [Medium](#), 900 mL

$L$  = Tablet label claim (mg)

**Tolerances:** NLT 75% ( $Q$ ) of the labeled amount of  $C_{32}H_{39}NO_4 \cdot HCl$  is dissolved.

**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 min

**Buffer solution:** 6.64 g/L of [monobasic sodium phosphate monohydrate](#) and 0.84 g/L of [sodium perchlorate monohydrate](#) in [water](#). Add 4 mL/L of [triethylamine](#). Adjust with [phosphoric acid](#) to a pH of  $2.3 \pm 0.1$ .

**Mobile phase:** *Buffer solution* and [acetonitrile](#) (65:35)

**Standard stock solution:** 0.5 mg/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.

**Standard solution:** Dilute the *Standard stock solution* with [Medium](#) to obtain a final concentration of 0.07 mg/mL of [USP Fexofenadine Hydrochloride RS](#). This solution is stable for 8 days under refrigeration or for 24 h at room temperature.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45- $\mu$ m pore size.

#### Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm  $\times$  10-cm; 5- $\mu$ m packing [L1](#)

**Column temperature:** 40°

**Flow rate:** 2.5 mL/min

**Injection volume:** 20  $\mu$ L

#### System suitability

**Sample:** Standard solution**Suitability requirements****Tailing factor:** NMT 2.0**Column efficiency:** NLT 1000 theoretical plates**Relative standard deviation:** NMT 2.0%

Calculate the percentage of fexofenadine hydrochloride dissolved in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times (C_s/L) \times V \times 100$$

 $r_u$  = peak response from the *Sample solution* $r_s$  = peak response from the *Standard solution* $C_s$  = concentration of the *Standard solution* (mg/mL) $L$  = Tablet label claim (mg) $V$  = volume of *Medium*, 900 or 1800 mL**Tolerances:** NLT 75% (Q) of the labeled amount of fexofenadine hydrochloride is dissolved.**Test 4:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 4*.**Medium:** 0.001 N [hydrochloric acid](#); 900 mL, degassed**Apparatus 2:** 75 rpm**Time:** 15 min**Buffer solution:** 6.64 g/L of [monobasic sodium phosphate monohydrate](#) and 0.84 g/L of [sodium perchlorate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.0.**Mobile phase:** [Acetonitrile](#), [Buffer solution](#), and [triethylamine](#) (50: 50: 0.3)**Standard stock solution:** 0.55 mg/mL of [USP Fexofenadine Hydrochloride RS](#) in 0.01 N [hydrochloric acid](#)**Standard solution:** Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of 0.22 mg/mL of [USP Fexofenadine Hydrochloride RS](#). Pass a portion of the solution through a suitable filter of 0.45- $\mu$ m pore size.**Sample solution:** Pass a portion of the solution under test through a suitable filter.**Chromatographic system**(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 220 nm**Column:** 4.6-mm  $\times$  25-cm; 5- $\mu$ m packing [L11](#)**Column temperature:** 25°**Flow rate:** 1.5 mL/min**Injection volume:** 20  $\mu$ L**Run time:** NLT 2.7 times the retention time of fexofenadine**System suitability****Sample:** Standard solution**Suitability requirements****Tailing factor:** NMT 2.0**Relative standard deviation:** NMT 1.0%**Analysis****Samples:** Standard solution and Sample solutionCalculate the percentage of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) dissolved in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times C_s \times V \times (1/L) \times 100$$

 $r_u$  = peak response from the *Sample solution* $r_s$  = peak response from the *Standard solution* $C_s$  = concentration of the *Standard solution* (mg/mL) $V$  = volume of *Medium*, 900 mL $L$  = label claim (mg/Tablet)**Tolerances:** NLT 80% (Q) of the labeled amount of fexofenadine hydrochloride ( $C_{32}H_{39}NO_4 \cdot HCl$ ) is dissolved.

- [Uniformity of Dosage Units \(905\)](#): Meet the requirements

**IMPURITIES****Change to read:**

• **PROCEDURE**

**Solution A, Solution B, Diluent, Mobile phase, Standard stock solution, Sample stock solution, and Sample solution:** Prepare as directed in the Assay.

**Standard solution:** 0.015 mg/mL of fexofenadine hydrochloride and 0.0045 mg/mL of fexofenadine related compound A from Quantitative limit solution and the Standard stock solution in Mobile phase

**System suitability stock solution:** Dilute 4.0 mL of the Standard stock solution with Mobile phase to 100 mL.

**System suitability solution:** Dilute 6.0 mL of the System suitability stock solution with Mobile phase to 100 mL.

**Quantitative limit solution:** 0.05 mg/mL of [USP Fexofenadine Related Compound A RS](#) in Diluent

**Chromatographic system**

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 25-cm; 5-μm packing [L11](#)

**Column temperature:** 35°

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 μL

**System suitability**

**Samples:** Standard solution and System suitability solution

[**NOTE**—For the relative retention times, see [Impurity Table 1](#).]

**Suitability requirements**

**Resolution:** NLT 7 between fexofenadine and fexofenadine related compound A, Standard solution

**Tailing factor:** NMT 2.0, Standard solution

**Relative standard deviation:** NMT 6%, System suitability solution; NMT 2.0% and NMT 3.0% for fexofenadine and fexofenadine related compound A, Standard solution

**Analysis**

**Samples:** Standard solution, Sample stock solution, and Sample solution

Calculate the percentage of fexofenadine related compound A in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

$r_u$  = peak area of fexofenadine related compound A in the Sample stock solution

$r_s$  = peak area of fexofenadine related compound A in the Standard solution

$C_s$  = concentration of fexofenadine related compound A in the Standard solution (mg/mL)

$C_u$  = concentration of fexofenadine hydrochloride in the Sample stock solution

Calculate the percentage of the decarboxylated degradant [( $\pm$ )-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-isopropylbenzene] 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 area of the decarboxylated degradant in the Sample stock solution

$r_s$  = peak area of fexofenadine in the Standard solution

$C_s$  = concentration of [USP Fexofenadine Hydrochloride RS](#) in the Standard solution (mg/mL)

$C_u$  = concentration of fexofenadine hydrochloride in the Sample stock solution

$F$  = relative response factor (see [Impurity Table 1](#))

Calculate the percentage of any other impurities in the portion of Tablets taken:

$$\text{Result} = r_u/(F \times r_s + r_T) \times 100$$

$r_u$  = peak area for each individual unknown impurity in the Sample stock solution

$F$  = difference in concentration between the Sample stock solution and the Sample solution, 66.7

$r_s$  = peak area response for fexofenadine in the Sample solution

$r_T$  = sum of the peak areas of all unknown impurities in the Sample stock solution

[**NOTE**—Disregard any peak below 0.05%.]

**Acceptance criteria****Individual impurities:** See [Impurity Table 1](#).**Total impurities:** NMT ▲1.3▲ (RB 1-May-2024)**Impurity Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fexofenadine related compound A	1.6	—	▲1.0▲ (RB 1-May-2024)
Decarboxylated degradant	6.7	1.1	0.15
Fexofenadine	1.0	—	—
Any individual other impurity	—	1.0	0.2

**ADDITIONAL REQUIREMENTS**

- 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](#)

2-(4-[4-(Hydroxydiphenylmethyl)piperidin-1-yl]butanoyl)phenyl)-2-methylpropanoic acid;

Also known as Benzeneacetic acid, 4-[1-oxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]- $\alpha,\alpha$ -dimethyl.**Auxiliary Information** - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
FEXOFENADINE HYDROCHLORIDE TABLETS	<a href="#">Documentary Standards Support</a>	SM52020 Small Molecules 5

**Chromatographic Database Information:** [Chromatographic Database](#)**Most Recently Appeared In:**

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