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Fexofenadine Hydrochloride Capsules

DEFINITION

Fexofenadine Hydrochloride Capsules contain NLT 93.0% and NMT 105.0% of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$).

IDENTIFICATION

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

Change to read:

• **B.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K▲ (CN 1-May-2020)

Sample solution: Empty an equivalent of 60 mg of fexofenadine hydrochloride, from the contents of several Capsules, into a suitable capped tube. Add 10 mL of a mixture of acetonitrile and methanol (10:1), and shake until the sample is dispersed. Allow to settle. Decant, filter, and collect the supernatant in a suitable beaker. Evaporate the solvent to near dryness by using a stream of nitrogen and with gentle heating from an appropriate source (steam, low-temperature hot plate). While still warm, add 5 mL of water and 5 drops of diluted hydrochloric acid, and stir to induce precipitation. Chill in an ice bath for about 30 min. Pass through a 10- to 15-µm filtering crucible with fritted disk. Dry the precipitate in an air oven for 1 h at 105°.

Acceptance criteria: Meet the requirements

ASSAY

• **Procedure**

Buffer: 6.64 g/L of monobasic sodium phosphate and 0.84 g/L of sodium perchlorate in water. Adjust with phosphoric acid to a pH of 2.0.

Diluent: Acetonitrile and *Buffer* (1:1)

Mobile phase: Acetonitrile and *Buffer* (7:13). Add 3 mL/L of triethylamine.

Standard solution: 0.06 mg/mL of USP Fexofenadine Hydrochloride RS and 0.005 mg/mL of USP Fexofenadine Related Compound A RS in *Mobile phase*

Sample stock solution: Remove, as completely as possible, the contents of NLT 20 Capsules, mix the combined contents, and finely powder by using a mortar and pestle. Transfer a portion of the powder, equivalent to about 50 mg of fexofenadine hydrochloride, to a 50-mL volumetric flask. Add 40 mL of *Diluent*, and shake by mechanical means for 60 min. Sonicate for about 2 min. Allow to cool to room temperature, and dilute with *Diluent* to volume.

Sample solution: Transfer 3.0 mL of the *Sample stock solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L11

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10 between fexofenadine and fexofenadine related compound A

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% and 3.0% for fexofenadine and fexofenadine related compound A, respectively

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) in the portion of Capsules 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 of fexofenadine 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%–105.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 15 and 45 min

Buffer: 1.0 g of monobasic sodium phosphate, 0.5 g of sodium perchlorate, and 0.3 mL of phosphoric acid in 300 mL of water

Mobile phase: Acetonitrile and *Buffer* (7:3)

System suitability stock solution: 0.44 mg/mL of USP Fexofenadine Related Compound A RS in water. [Note—A small amount of glacial acetic acid, not to exceed 5% of the total volume, may be used if necessary to dissolve USP Fexofenadine Related Compound A RS.]

System suitability solution: Prepare a solution of USP Fexofenadine Hydrochloride RS in the *System suitability stock solution* containing 0.01 mg/mL of USP Fexofenadine Related Compound A RS and 0.06 mg/mL of USP Fexofenadine Hydrochloride RS.

Standard solution: 0.07 mg/mL of USP Fexofenadine Hydrochloride RS in water. [Note—A small amount of methanol, not to exceed 0.5% of the total volume, may be used if necessary to dissolve USP Fexofenadine Hydrochloride RS.]

Sample solution: Filtered portions of the solution under test

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 10-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Samples: *System suitability solution* and *Standard 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 the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) dissolved.

Tolerances: NLT 50% (*Q*) of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) is dissolved in 15 min; NLT 75% (*Q*) of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) is dissolved in 45 min.

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

Medium, Apparatus, Buffer, Mobile phase, System suitability stock solution, System suitability solution, Chromatographic system, and **Analysis:** Proceed as directed for *Test 1*.

Time: 45 min

Tolerances: NLT 75% (*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

• **Organic Impurities**

Buffer: 6.64 mg/mL of monobasic sodium phosphate and 0.84 mg/mL of sodium perchlorate in water. Adjust with phosphoric acid to a pH of 2.0.

Diluent: Acetonitrile and *Buffer* (1:1)

Mobile phase: Acetonitrile and *Buffer* (7:13). Add 3 mL/L of triethylamine

Standard solution: 0.06 mg/mL of USP Fexofenadine Hydrochloride RS and 0.005 mg/mL of USP Fexofenadine Related Compound A RS in *Mobile phase*

Sample solution: Use the *Sample stock solution* as prepared in the *Assay*.

Reference solution: 0.06 mg/mL of fexofenadine hydrochloride in *Mobile phase* from the *Sample solution*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L11

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10 between fexofenadine and fexofenadine related compound A

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% and 3.0% for fexofenadine and fexofenadine related compound A, respectively

Analysis

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

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response for fexofenadine related compound A from the *Sample solution*

r_S = peak response for fexofenadine related compound A from the *Standard solution*

C_S = concentration of USP Fexofenadine Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of decarboxylated degradant [(±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-isopropylbenzene], with a relative retention time of 3.2, in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of the decarboxylated degradant from the *Sample solution*

r_S = peak response of fexofenadine from the *Standard solution*

C_S = concentration of USP Fexofenadine Hydrochloride RS in the *Standard solution* (mg/mL)

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

F = response factor for the decarboxylated degradant relative to fexofenadine, 1.1

Calculate the percentage of other impurities in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response for any other impurity from the *Sample solution*

r_S = peak response of fexofenadine from the *Reference solution*

C_S = concentration of fexofenadine in the *Reference solution* (mg/mL)

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Acceptance Criteria, NMT (%)
Fexofenadine related compound A[a]	0.4
Decarboxylated degradant[b]	0.2
Any other individual, unidentified impurity	0.2
Total impurities	0.5

[a] Benzeneacetic acid, 4-[1-oxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl.

[b] (±)-4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-isopropylbenzene.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. 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-[4-(Hydroxydiphenylmethyl)piperidin-1-yl]butanoyl}phenyl)-2-methylpropanoic acid;
Also known as Benzeneacetic acid, 4-[1-oxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl.
$C_{32}H_{37}NO_4$ 499.65

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FEXOFENADINE HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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