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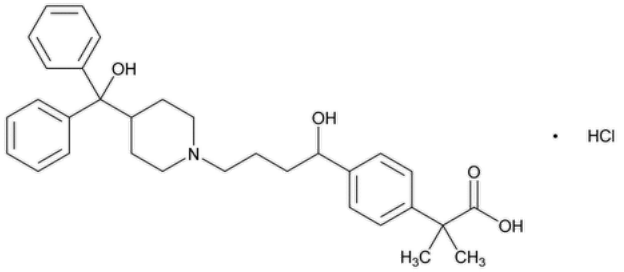
Fexofenadine Hydrochloride



$C_{32}H_{39}NO_4 \cdot HCl$ 538.12

Benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxy diphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl-, hydrochloride, (±)-;
(±)-*p*-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)piperidino]butyl]-α-methylhydratropic acid, hydrochloride CAS RN®: 153439-40-8; UNII: 2S068B75ZU.

DEFINITION

Fexofenadine Hydrochloride contains NLT 98.0% and NMT 102.0% of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **B.** The retention time of the fexofenadine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.**

Analysis: Examine the precipitate formed in *Other Components* for the *Content of Chloride* test.

Acceptance criteria: A white precipitate is observed.

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: 1.0 mg/mL of Fexofenadine Hydrochloride in *Diluent*

Sample solution: 0.06 mg/mL of Fexofenadine Hydrochloride in *Mobile phase* from the *Sample stock 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% for fexofenadine and NMT 3.0% for fexofenadine related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) in the portion of Fexofenadine Hydrochloride 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 = concentration of Fexofenadine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

OTHER COMPONENTS

• **Content of Chloride**

Sample: 300 mg of Fexofenadine Hydrochloride

Blank: Methanol

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometrically

Analysis: Dissolve the *Sample* in 50 mL of methanol. Each mL of 0.1 N silver nitrate VS is equivalent to 3.545 mg of chloride.

Acceptance criteria: 6.45%–6.75% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Limit of Fexofenadine Related Compound B**

Buffer: Glacial acetic acid and water (2.3: 2000). Adjust with 6 N ammonium hydroxide to a pH of 4.0 ± 0.1.

Mobile phase: Acetonitrile and *Buffer* (20:80)

System suitability solution: Add 1.2 mg of USP Fexofenadine Related Compound B RS to a 5-mL volumetric flask. Dilute with *Mobile phase* to volume. Transfer 2.0 mL of the solution into a 100-mL volumetric flask. Add 25 mg of USP Fexofenadine Hydrochloride RS, and dilute with *Mobile phase* to volume.

Standard solution: 2.5 µg/mL of USP Fexofenadine Hydrochloride RS in *Mobile phase* from the *System suitability solution*

Sample solution: 0.25 mg/mL of Fexofenadine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L45

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for fexofenadine related compound B and fexofenadine are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and fexofenadine related compound B

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fexofenadine related compound B in the portion of Fexofenadine Hydrochloride taken:

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

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

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

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

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

F = relative response factor for fexofenadine related compound B relative to fexofenadine, 0.8

Acceptance criteria: NMT 0.2%

• **Other Organic Impurities**

Buffer, Diluent, Mobile phase, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

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

Reference solution: Use the *Sample solution* in the *Assay*.

Samples: *Standard solution*, *Sample solution*, *Reference solution*, and *Mobile phase* (used as the blank)

Measure the peak areas, excluding the peaks corresponding to those from the *Mobile phase*.

Calculate the percentage of fexofenadine related compound A in the portion of Fexofenadine Hydrochloride 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 = 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 Fexofenadine Hydrochloride 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 = concentration of fexofenadine in the *Sample solution* (mg/mL)

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

Calculate the percentage of other impurities in the portion of Fexofenadine Hydrochloride 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 = 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]	0.2
Decarboxylated degradant[b]	0.15
Any other individual, unidentified impurity	0.1
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.

SPECIFIC TESTS

• **Water Determination,** *Method Ic* ⟨921⟩**:** NMT 2.0% for the anhydrous form; 6.0%–10.0% for the hydrate form. [Note—"Hydrate" refers to a mixture of dihydrate and trihydrate forms of fexofenadine hydrochloride.]

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store at controlled room temperature.

• **Labeling:** Where it is the hydrate form, the label so indicates.

Change to read:

• **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

USP Fexofenadine Related Compound B RS

3-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl benzeneacetic acid hydrochloride ▲monohydrate;
Also known as 2-(3-{1-Hydroxy-4-[4-(hydroxydiphenylmethyl)piperidin-1-yl]butyl}phenyl)-2-methylpropanoic acid hydrochloride monohydrate.▲

(ERR 1-Feb-2021)

$C_{32}H_{39}NO_4 \cdot HCl$▲ $\cdot H_2O$ 556.14▲ (ERR 1-Feb-2021)

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

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

Chromatographic Database Information: Chromatographic Database

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