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Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Extended-Release Tablets

DEFINITION

Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Extended-Release Tablets contain NLT 93.0% and NMT 107.0% of the labeled amounts of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** The retention times of the ▲fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024) peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **B.** **Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution A: 6 mg/mL of USP Fexofenadine Hydrochloride RS in methanol

Standard solution B: 12 mg/mL of USP Pseudoephedrine Hydrochloride RS in methanol

Sample solution: ▲Nominally 6 mg/mL of fexofenadine hydrochloride and 12 mg/mL of pseudoephedrine hydrochloride from Tablets prepared as follows.▲ (IRA 1-Nov-2024) Transfer the equivalent of 30 mg of fexofenadine hydrochloride and 60 mg of pseudoephedrine hydrochloride from finely powdered Tablets (NLT 4) into a suitable vessel, and add 5 mL of methanol. Cap the vessel, and shake vigorously for 2 min. Pass the resulting suspension through a suitable filter of 0.45-µm pore size. Use the filtrate.

Adsorbent: 0.2-mm layer of HPTLC silica gel mixture. Dry the plate at 105° for 1 h before use.

Application volume: 10 µL

Developing solvent system: Toluene, dehydrated alcohol, and ammonium hydroxide (50:45:5)

Analysis: Proceed as directed, using the *Developing solvent system*. After removal of the plate, mark the solvent front, and allow the plate to air-dry. Heat the plate at 105° until the odor of ammonia disappears (about 5 min). Allow the plate to cool, and examine under UV light at 254 nm.

[Note—The R_F values for fexofenadine and pseudoephedrine are 0.17 and 0.39, respectively.]

Acceptance criteria: The R_F value of fexofenadine hydrochloride in the *Sample solution* is comparable to that of fexofenadine hydrochloride in *Standard solution A*. The R_F value of pseudoephedrine hydrochloride in the *Sample solution* is comparable to that of pseudoephedrine hydrochloride in *Standard solution B*.

ASSAY

Change to read:

• **Procedure 1**

Buffer: Dissolve 6.8 g of sodium acetate and 16.22 g of sodium 1-octanesulfonate in water, and dilute with water to 1 L. Adjust with glacial acetic acid to a pH of 4.6.

Mobile phase: Methanol and *Buffer* ▲(65:35)▲ (IRA 1-Nov-2024)

System suitability solution: Transfer 40 mg of USP Pseudoephedrine Hydrochloride RS to a 50-mL volumetric flask. Add 5 mL of *tert*-butylhydroperoxide solution, and sonicate. Cover the flask opening with aluminum foil, and place the flask in an oven at 90° for 60 min. Remove from the oven, and allow to cool. Add 35 mL of *Mobile phase*, and cool to room temperature. Dilute with *Mobile phase* to volume. The degradation of pseudoephedrine hydrochloride by this process produces the related compound ▲methcathinone.▲ (IRA 1-Nov-2024)

Related compounds stock solution: ▲0.2 mg/mL each of USP Fexofenadine Related Compound A RS and USP Fexofenadine Related Compound C RS prepared as follows. Transfer suitable▲ (IRA 1-Nov-2024) quantities of USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS to a suitable volumetric flask. Dissolve in 65% of the flask volume of methanol and dilute with *Buffer* to volume.▲ (IRA 1-Nov-2024)

Related compounds solution: 0.02 mg/mL each of USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS▲ (IRA 1-Nov-2024) from *Related compounds stock solution* ▲in▲ (IRA 1-Nov-2024) *Mobile phase*

Standard stock solution: 0.4 mg/mL of ▲▲ (IRA 1-Nov-2024) USP Fexofenadine Hydrochloride RS and ▲0.8 mg/mL of ▲ (IRA 1-Nov-2024) USP Pseudoephedrine Hydrochloride RS, ▲▲ (IRA 1-Nov-2024) in *Mobile phase*

Standard solution: ▲0.048 mg/mL of USP Fexofenadine Hydrochloride RS and 0.096 mg/mL of USP Pseudoephedrine Hydrochloride RS from the *Standard stock solution*, and 0.006 mg/mL each of USP Fexofenadine Related Compound A RS and USP Fexofenadine Related Compound C RS from the *Related compounds solution* in *Mobile phase*▲ (IRA 1-Nov-2024)

Sample stock solution: Nominally ▲▲ (IRA 1-Nov-2024) 1.2 mg/mL of fexofenadine hydrochloride and 2.4 mg/mL of pseudoephedrine hydrochloride ▲from Tablets prepared as follows.▲ (IRA 1-Nov-2024) Transfer NLT 10 whole Tablets to a 500-mL volumetric flask. Add 300 mL of methanol, and shake by mechanical means at high speed for 60 min. Sonicate the flask for 60 min at 40°. Add 150 mL of *Buffer*, and sonicate for 60 min at 40°. Vent the flask, and vigorously shake the flask by hand at 15-min intervals during the mechanical shaking and sonication steps. Cool to room temperature, and dilute with *Buffer* to volume. ▲▲ (IRA 1-Nov-2024) Pass a portion of this solution through a filter of 0.45-µm or finer pore size, and use the filtrate. ▲[NOTE—Alternatively, centrifuge the *Sample stock solution*, and use the supernatant to prepare the *Sample solution*.]▲ (IRA 1-Nov-2024)

Sample solution: ▲Nominally▲ (IRA 1-Nov-2024) 0.048 and 0.096 mg/mL of fexofenadine hydrochloride and pseudoephedrine hydrochloride, respectively, from the *Sample stock solution*▲in▲ (IRA 1-Nov-2024) *Mobile phase*. ▲Filter the *Sample solution* before analysis.▲ (IRA 1-Nov-2024)

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 5-cm; 5-µm packing L6 connected in series to a 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: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for pseudoephedrine and ▲methcathinone▲ (IRA 1-Nov-2024) are 1.0 and 1.2, respectively (*System suitability solution*); and for fexofenadine, fexofenadine related compound A, and ▲fexofenadine related compound C are▲ (IRA 1-Nov-2024) 1.0, 1.2, and ▲2.3,▲ (IRA 1-Nov-2024) respectively (*Standard solution*).]

Suitability requirements

Resolution: NLT 1.5 between pseudoephedrine and ▲methcathinone,▲ (IRA 1-Nov-2024) *System suitability solution*; NLT 2.0 between fexofenadine and fexofenadine related compound A, *Standard solution*

Relative standard deviation: NMT 1.0% for ▲▲ (IRA 1-Nov-2024) pseudoephedrine, ▲*Standard solution*;▲ (IRA 1-Nov-2024) NMT 1.0% for ▲▲ (IRA 1-Nov-2024) fexofenadine▲ (IRA 1-Nov-2024) , *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate ▲▲ (IRA 1-Nov-2024) the percentage of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of ▲▲ (IRA 1-Nov-2024) fexofenadine or pseudoephedrine from the *Sample solution*

r_S = peak response of ▲▲ (IRA 1-Nov-2024) fexofenadine or pseudoephedrine from the *Standard solution*

C_S = concentration of ▲▲ (IRA 1-Nov-2024) USP Fexofenadine Hydrochloride RS or USP Pseudoephedrine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ▲▲ (IRA 1-Nov-2024) fexofenadine hydrochloride or pseudoephedrine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

Change to read:

• **PROCEDURE 2:** Use this procedure for Tablets labeled to meet *Dissolution Test 5*.

Buffer: Dissolve 6.8 g of sodium acetate and 16.22 g of sodium 1-octanesulfonate in water, and dilute with water to 1 L. Adjust with glacial acetic acid to a pH of 4.0.

Mobile phase: Methanol and *Buffer* ▲(65:35)▲ (IRA 1-Nov-2024)

System suitability solution: Transfer 60 mg of USP Pseudoephedrine Hydrochloride RS to a 50-mL volumetric flask. Add 10 mL of hydrogen peroxide, and swirl the flask. Cover the flask opening with aluminum foil, and heat in an oven at 90° for 4 h. Add 35 mL of *Mobile phase*, and cool to room temperature. Dilute with *Mobile phase* to volume. The degradation of pseudoephedrine hydrochloride by this process produces the related compound ▲methcathinone.▲ (IRA 1-Nov-2024)

Related compounds stock solution: 0.225 mg/mL each of USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS,▲ (IRA 1-Nov-2024) prepared as follows. ▲Transfer suitable quantities of▲ (IRA 1-Nov-2024) USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS to a suitable volumetric flask. Dissolve in 65% of the flask volume of methanol and dilute with *Buffer* to volume.▲ (IRA 1-Nov-2024)

Related compounds solution: 0.0113 mg/mL each of USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS▲ (IRA 1-Nov-2024) from *Related compounds stock solution* in *Mobile phase*

Standard stock solution: 0.36 mg/mL of USP Fexofenadine Hydrochloride RS and 0.48 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Mobile phase*

Standard solution: 0.096 mg/mL of USP Pseudoephedrine Hydrochloride RS, 0.072 mg/mL of USP Fexofenadine Hydrochloride RS▲from the *Standard stock solution*,▲ (IRA 1-Nov-2024) and 0.002 mg/mL each of USP Fexofenadine Related Compound A RS and ▲USP Fexofenadine Related Compound C RS from the *Related compounds solution* in *Mobile phase*▲ (IRA 1-Nov-2024)

Sample stock solution: Nominally ▲▲ (IRA 1-Nov-2024) 0.36 mg/mL of fexofenadine hydrochloride and 0.48 mg/mL of pseudoephedrine hydrochloride ▲from Tablets,▲ (IRA 1-Nov-2024) prepared as follows. Crush NLT 10 Tablets into small pieces in a mortar, transfer the composite to a 500-mL volumetric flask, and add 325 mL of methanol. Shake by mechanical means for at least 30 min, and sonicate for at least an additional 35 min. Add 100 mL of *Buffer*, sonicate for 45 min, cool to room temperature, and allow to stand for 16 h without mechanical shaking. Dilute with *Buffer* to volume. Pass a portion of this solution through a suitable filter of 0.45-µm or finer pore size. Transfer 5 mL of the filtrate to a 50-mL volumetric flask, and dilute with *Buffer* to volume.

Sample solution: ▲Nominally▲ (IRA 1-Nov-2024) 0.072 and 0.096 mg/mL of fexofenadine hydrochloride and pseudoephedrine hydrochloride, respectively, 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 × 5-cm; 5-µm packing L6 connected in series to a 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: *System suitability solution* and *Standard solution*

▲[NOTE—The relative retention times for pseudoephedrine and methcathinone are 1.0 and 1.2, respectively, *System suitability solution*; and for fexofenadine, fexofenadine related compound A, and fexofenadine related compound C are 1.0, 1.2, and 2.3, respectively, *Standard solution*.]▲ (IRA 1-Nov-2024)

Suitability requirements

Resolution: NLT 2.0 between pseudoephedrine and ▲methcathinone,▲ (IRA 1-Nov-2024) *System suitability solution*; NLT 2.0 between fexofenadine and fexofenadine related compound A, *Standard solution*

Relative standard deviation: NMT 1.0% for ▲▲ (IRA 1-Nov-2024) pseudoephedrine, ▲*Standard solution*;▲ (IRA 1-Nov-2024) NMT 1.0% for ▲▲ (IRA 1-Nov-2024) fexofenadine, ▲▲ (IRA 1-Nov-2024) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate ▲▲ (IRA 1-Nov-2024) the percentage of the labeled amount of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of ▲▲ (IRA 1-Nov-2024) fexofenadine or pseudoephedrine from the *Sample solution*

r_S = peak response of ▲▲ (IRA 1-Nov-2024) fexofenadine or pseudoephedrine from the *Standard solution*

C_S = concentration of ▲▲ (IRA 1-Nov-2024) USP Fexofenadine Hydrochloride RS or USP Pseudoephedrine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ▲▲ (IRA 1-Nov-2024) fexofenadine hydrochloride or pseudoephedrine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.001 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Times

Fexofenadine hydrochloride: 15 and 45 min

Pseudoephedrine hydrochloride: 45 min; 3, 5, and 12 h

Solution A: 7.0 ▲g/L▲ (IRA 1-Nov-2024) of monobasic sodium phosphate monohydrate in water. Adjust with ▲▲ (IRA 1-Nov-2024) phosphoric acid to a pH of 2.00 ± 0.05.

Mobile phase: Acetonitrile and *Solution A* ▲(45:55)▲ (IRA 1-Nov-2024)

Standard solution: Dissolve quantities of USP Fexofenadine Hydrochloride RS and USP Pseudoephedrine Hydrochloride RS in *Medium*, and dilute to obtain a solution containing known concentrations similar to those expected in the *Sample solution*. [Note—A small amount of methanol, NMT 0.5% of the total volume, can be used to dissolve the fexofenadine hydrochloride.]

Sample solution: Pass a portion of the solution under test through a suitable nylon filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; packing L6

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 1.5 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 2.0% ▲for fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of the labeled amounts of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved.

Tolerances

Fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$)**:** NLT 65% (*Q*) of the labeled amount is dissolved in 15 min, and NLT 80% (*Q*) of the labeled amount is dissolved in 45 min.

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 1*.

Table 1

Time	Amount Dissolved (%)
45 min	NMT 36
3 h	45–69
5 h	61–80
12 h	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

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

Times

Fexofenadine hydrochloride: 45 min

Pseudoephedrine hydrochloride: 30 min; 2, 4, and 12 h

Solution A: 2.7 ▲g/L▲ (IRA 1-Nov-2024) of monobasic potassium phosphate and 2.2 ▲g/L▲ (IRA 1-Nov-2024) of sodium 1-octanesulfonate in water. Adjust with phosphoric acid to a pH of 2.50 ± 0.05.

Mobile phase: Methanol, acetonitrile, and *Solution A* ▲(30:30:40)▲ (IRA 1-Nov-2024)

Fexofenadine standard stock solution: Transfer 66 mg of USP Fexofenadine Hydrochloride RS to a 100-mL volumetric flask. Add 10 mL of methanol, and swirl until dissolved. Add 50 mL of *Medium*, and mix. Allow the solution to equilibrate to room temperature, and dilute with *Medium* to volume.

Pseudoephedrine standard stock solution: Transfer 66 mg of USP Pseudoephedrine Hydrochloride RS to a 100-mL volumetric flask. Add 10 mL of methanol, and swirl until dissolved. Add 50 mL of *Medium*, and mix. Allow the solution to equilibrate to room temperature, and dilute with *Medium* to volume.

Standard solution: 66 µg/mL of USP Fexofenadine Hydrochloride RS and 132 µg/mL of USP Pseudoephedrine Hydrochloride RS from ▲▲ (IRA 1-Nov-2024) *Fexofenadine standard stock solution* and *Pseudoephedrine standard stock solution* ▲respectively, in▲ (IRA 1-Nov-2024) *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 2.0 for fexofenadine and NMT 2.5 for pseudoephedrine

Relative standard deviation: NMT 2.0% for ▲fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of the labeled amounts of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved.

Tolerances

Fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$)**:** NLT 80% (*Q*) of the labeled amount is dissolved in 45 min.

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 2*.

Table 2

Time	Amount Dissolved (%)
30 min	NMT 35
2 h	38–58
4 h	56–76
12 h	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

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

Apparatus 2: 50 rpm

Times

Fexofenadine hydrochloride: 30 min

Pseudoephedrine hydrochloride: ▲30 min;▲ (IRA 1-Nov-2024) 2, 4, and 12 h

Buffer solution: 6.64 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 2.50 ± 0.05.

Mobile phase: ▲Acetonitrile and *Buffer solution* (40:60)▲ (IRA 1-Nov-2024)

Standard solution: [NOTE—A small amount of methanol, not exceeding 0.5% of the final total volume, can be used to dissolve fexofenadine hydrochloride.] Prepare a solution in *Medium* containing known concentrations of USP Fexofenadine Hydrochloride RS and USP Pseudoephedrine Hydrochloride RS similar to those expected in the solution under test.

Sample solution: Pass a portion of the solution under test through a suitable PVDF or nylon filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 2.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 2.0% for ▲fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of the labeled amounts of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved.

Tolerances

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

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 3*.

Table 3

Time ▲▲ (IRA 1-Nov-2024)	Amount Dissolved (%)
▲30 min▲ (IRA 1-Nov-2024)	13–33
2 ▲h▲ (IRA 1-Nov-2024)	35–55
4 ▲h▲ (IRA 1-Nov-2024)	50–70
12 ▲h▲ (IRA 1-Nov-2024)	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

Test 4: For products labeled with a dosing interval of 24 h. 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

Apparatus 2: 50 rpm

Times

Fexofenadine hydrochloride: 30 min

Pseudoephedrine hydrochloride: 3, 7, and 23 h

Determine the percentages of the labeled amounts of fexofenadine hydrochloride and pseudoephedrine hydrochloride dissolved by using the chromatographic procedure described in *Test 1*.

Tolerances

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

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 4*.

Table 4

Time (h)	Amount Dissolved (%)
3	10–30
7	35–65
23	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 5: For products labeled with a dosing interval of 24 h. If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 5*.

Medium: 0.001 N hydrochloric acid; 900 mL deaerated

Apparatus 2: 50 rpm, with sinkers[1]

Times

Fexofenadine hydrochloride: 15 and 45 min

Pseudoephedrine hydrochloride: 3, 7, and 23 h

Buffer: 4.1 g/L of anhydrous sodium acetate in water. Adjust with glacial acetic acid to a pH of 3.6 ± 0.1.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: Prepare a solution in *Medium* containing 0.20 mg/mL of USP Fexofenadine Hydrochloride RS and 0.27 mg/mL of USP Pseudoephedrine Hydrochloride RS. Sonicate to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 10-cm; 5-µm packing L9

Column temperature: 40°

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for fexofenadine and pseudoephedrine are 0.45 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 2.0 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 1.5% for fexofenadine and pseudoephedrine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) ▲▲ (IRA 1-Nov-2024) :

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

r_U = peak response of fexofenadine 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)

Calculate the percentage of the labeled amount ▲▲ (IRA 1-Nov-2024) of fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$) dissolved at each time point (i) ▲▲ (IRA 1-Nov-2024) :

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

C_i = concentration of fexofenadine hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for fexofenadine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Calculate the concentration (C_i) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) ▲▲ (IRA 1-Nov-2024) :

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

r_U = peak response of pseudoephedrine from the *Sample solution*

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

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

Calculate the percentage of the labeled amount ▲▲ (IRA 1-Nov-2024) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved at each time point (i) ▲▲ (IRA 1-Nov-2024) :

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of pseudoephedrine hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for pseudoephedrine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Tolerances

Fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$)**:** See *Table 5*.

Table 5

Time Point (*i*)	Time (min)	Amount Dissolved (%)
1	15	NLT 60 (*Q*)
2	45	NLT 75 (*Q*)

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 6*.

Table 6

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	3	10–34
2	7	35–68
3	23	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 6: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 6*.

Medium: 0.001 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Times

Fexofenadine hydrochloride: 45 min

Pseudoephedrine hydrochloride: 30 min; 2, 4, and 12 h

Solution A: 7 g/L of monobasic sodium phosphate in water. Adjust with ▲▲ (IRA 1-Nov-2024) phosphoric acid to a pH of 2.00.

Mobile phase: Acetonitrile and *Solution A* (45:55)

Standard solution: 0.07 mg/mL of USP Fexofenadine Hydrochloride RS and 0.13 mg/mL of USP Pseudoephedrine Hydrochloride RS, prepared as follows. Dissolve appropriate quantities of USP Fexofenadine Hydrochloride RS and USP Pseudoephedrine Hydrochloride RS in a small amount of methanol, NMT 0.8% of the final volume, and add 40% of the final volume of *Medium*. Sonicate to dissolve and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L6

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and pseudoephedrine ▲▲ (IRA 1-Nov-2024)

Tailing factor: NMT 2.0 for ▲▲ (IRA 1-Nov-2024) fexofenadine and pseudoephedrine ▲▲ (IRA 1-Nov-2024)

Relative standard deviation: NMT 2.0% for ▲fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024)

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:

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

r_U = peak response of fexofenadine 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)

V = volume of *Medium*, 900 mL

L = label claim for fexofenadine hydrochloride (mg/Tablet)

Calculate the concentration (C_i) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) ▲▲ (IRA 1-Nov-2024) :

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

r_U = peak response of pseudoephedrine from the *Sample solution*

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

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

Calculate the percentage of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved at each time point (i) ▲▲ (IRA 1-Nov-2024) :

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of pseudoephedrine hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for pseudoephedrine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Tolerances

Fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$)**:** NLT 80% (*Q*) of the labeled amount is dissolved.

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 7*.

Table 7

Time Point (*i*)	Time ▲▲ (IRA 1-Nov-2024)	Amount Dissolved (%)
1	▲30 min▲ (IRA 1-Nov-2024)	NMT 35
2	2 ▲h▲ (IRA 1-Nov-2024)	45–65
3	4 ▲h▲ (IRA 1-Nov-2024)	60–80
4	12 ▲h▲ (IRA 1-Nov-2024)	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 7: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 7*.

Medium: 0.001 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Times

Fexofenadine hydrochloride: 20 min

Pseudoephedrine hydrochloride: 45 min; 3, 5, and 12 h

Solution A: 7.0 g/L of monobasic sodium phosphate monohydrate in water. Adjust with phosphoric acid to a pH of 2.0.

Mobile phase: Acetonitrile and *Solution A* (45:55)

Standard stock solution A: 0.7 mg/mL of USP Fexofenadine Hydrochloride RS, prepared as follows. Transfer a quantity of USP Fexofenadine Hydrochloride RS to a suitable volumetric flask. Add methanol, NMT 5% of the ▲flask▲ (IRA 1-Nov-2024) volume, and sonicate to dissolve. Dilute with *Medium* to volume.

Standard stock solution B: 1.3 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Medium*. Sonicate to dissolve if necessary.

Standard solution: 0.07 mg/mL of USP Fexofenadine Hydrochloride RS and 0.13 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Medium*, from *Standard stock solution A* and *Standard stock solution B*

Sample solution: Withdraw and pass a portion of the solution under test through a suitable nylon filter of 0.45-µm pore size. Replace the portion removed with the same volume of *Medium*.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L6

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of ▲▲ (IRA 1-Nov-2024) pseudoephedrine▲▲ (IRA 1-Nov-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 1.5 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 2.0% ▲for fexofenadine and pseudoephedrine▲ (IRA 1-Nov-2024)

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:

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

r_U = peak response of fexofenadine 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)

V = volume of *Medium*, 900 mL

L = label claim for fexofenadine hydrochloride (mg/Tablet)

Calculate the concentration (C_i) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the sample withdrawn from the vessel at each time point (i) ▲▲ (IRA 1-Nov-2024) :

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

r_U = peak response of pseudoephedrine from the *Sample solution*

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

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

[NOTE—Result_1 is used as calculation correction (C_1) for subsequent withdrawal time points.]

Calculate the percentage of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved at each time point (i) ▲▲ (IRA 1-Nov-2024) :

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_5 = \{(C_5 \times V) + [(C_4 + C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of pseudoephedrine hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for pseudoephedrine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Tolerances

Fexofenadine hydrochloride ($C_{32}H_{39}NO_4 \cdot HCl$)**:** NLT 80% ($Q$) of the labeled amount is dissolved in 20 min.

Pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)**:** See *Table 8*.

Table 8

Time Point (i)	Time	Amount Dissolved (%)
1[a]	20 min	—
2	45 min	NMT 34
3	3 h	41–61
4	5 h	57–77
5	12 h	NLT 80

[a] The first time point is used as calculation correction (C_1) for subsequent withdrawal time points.

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 8: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 8*.

Medium: 0.001 N hydrochloric acid; 900 mL

Apparatus 1: 10-mesh basket, 100 rpm

Times

Fexofenadine hydrochloride: 20 min

Pseudoephedrine hydrochloride: 3, 7, and 23 h

Buffer: 7.0 g of monobasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.0.

Mobile phase: Acetonitrile and *Buffer* (45:55)

Standard solution: 0.2 mg/mL of USP Fexofenadine Hydrochloride RS and 0.27 mg/mL of USP Pseudoephedrine Hydrochloride RS, prepared as follows. Transfer a quantity of USP Fexofenadine Hydrochloride RS and USP Pseudoephedrine Hydrochloride RS to a suitable volumetric flask, and add 0.8% of the flask volume of methanol. Add 40% of the flask volume of the *Medium* and sonicate to dissolve. Dilute with *Medium* to volume.

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 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L6

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.7 times the retention time of the pseudoephedrine peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 2.0 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 2.0% for fexofenadine and pseudoephedrine

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:

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

r_U = peak response of fexofenadine 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)

V = volume of *Medium*, 900 mL

L = label claim for fexofenadine hydrochloride (mg/Tablet)

Determine the concentration (C_i) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of pseudoephedrine from the *Sample solution*

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

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

Calculate the percentage of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of pseudoephedrine hydrochloride in the portion of sample withdrawn at each time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for pseudoephedrine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: For Tablets labeled to contain 180 mg of fexofenadine hydrochloride and 240 mg of pseudoephedrine hydrochloride.

Fexofenadine hydrochloride: NLT 80% (Q) of the labeled amount is dissolved in 20 min.

Pseudoephedrine hydrochloride: See *Table 9*.

Table 9

Time Point (i)	Time	Amount Dissolved (%)
1[a]	20 min	—
2	3 h	10–30
3	7 h	40–60
4	23 h	NLT 80

[a] The first time point is used as calculation correction (C_1) for subsequent withdrawal time points.

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 9: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 9*.

Medium: 0.001 N hydrochloric acid; 900 mL

Apparatus 2

Fexofenadine hydrochloride: 50 rpm

Pseudoephedrine hydrochloride: 50 rpm, with suitable sinkers

Times

Fexofenadine hydrochloride: 30 min

Pseudoephedrine hydrochloride: 30 min; 2, 4, and 12 h

Buffer: 7.0 g of monobasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.0.

Mobile phase: Acetonitrile and *Buffer* (45:55)

Standard stock solution A: 0.7 mg/mL of USP Fexofenadine Hydrochloride RS, prepared as follows. Transfer a quantity of USP Fexofenadine Hydrochloride RS to a suitable volumetric flask. Add 8% of the flask volume of methanol and sonicate to dissolve. Dilute with *Medium* to volume.

Standard stock solution B: 1.3 mg/mL of USP Pseudoephedrine Hydrochloride RS, prepared as follows. Transfer a quantity of USP Pseudoephedrine Hydrochloride RS to a suitable volumetric flask. Add 8% of the flask volume of methanol and sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: 0.07 mg/mL of USP Fexofenadine Hydrochloride RS and 0.13 mg/mL of USP Pseudoephedrine Hydrochloride RS from *Standard stock solution A* and *Standard stock solution B* in *Medium*

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 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L6

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of the pseudoephedrine peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between fexofenadine and pseudoephedrine

Tailing factor: NMT 2.0 for fexofenadine and pseudoephedrine

Relative standard deviation: NMT 2.0% for fexofenadine and pseudoephedrine

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:

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

r_U = peak response of fexofenadine 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)

V = volume of *Medium*, 900 mL

L = label claim for fexofenadine hydrochloride (mg/Tablet)

Determine the concentration (C_i) of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of pseudoephedrine from the *Sample solution*

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

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

Calculate the percentage of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of pseudoephedrine hydrochloride in the portion of sample withdrawn at each time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for pseudoephedrine hydrochloride (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: For Tablets labeled to contain 60 mg of fexofenadine hydrochloride and 120 mg of pseudoephedrine hydrochloride.

Fexofenadine hydrochloride: NLT 80% (Q) of the labeled amount is dissolved in 30 min.

Pseudoephedrine hydrochloride: See *Table 10*.

Table 10

Time Point (i)	Time	Amount Dissolved (%)
1	30 min	8–28
2	2 h	34–54
3	4 h	56–76
4	12 h	NLT 80

The percentages of the labeled amount of pseudoephedrine hydrochloride, dissolved at the times specified, conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

[Note—On the basis of knowledge of the product, perform either: (a) *Organic Impurities, Procedure 1* or (b) *Organic Impurities, Procedure 2*; *Organic Impurities, Procedure 3*; and *Organic Impurities, Procedure 4*.]

Change to read:

• **Organic Impurities, Procedure 1**

Buffer, Mobile phase, ▲ (IRA 1-Nov-2024) **System suitability solution, Related compounds stock solution, Related compounds solution, Standard stock solution, Standard solution,** and **Chromatographic system:** Proceed as directed in the *Assay, Procedure 1*.

▲**Sensitivity solution:** 1.2 µg/mL of USP Fexofenadine Hydrochloride RS and 2.4 µg/mL of USP Pseudoephedrine Hydrochloride RS from the *Standard stock solution* in *Mobile phase*▲ (IRA 1-Nov-2024)

Sample solution: ▲Nominally 1.2 mg/mL of fexofenadine hydrochloride and 2.4 mg/mL of pseudoephedrine hydrochloride from Tablets prepared as follows. Transfer whole Tablets (NLT 10) to a 500-mL volumetric flask. Add 300 mL of methanol and shake by mechanical means at high speed for 60 min. Sonicate the flask for 60 min at 40°. Add 150 mL of *Buffer* and sonicate for 60 min at 40°. Vent the flask, and vigorously shake the flask by hand at 15-min intervals during the mechanical shaking and sonication steps. Cool to room temperature and dilute with *Buffer* to volume. Pass a portion of this solution through a filter of 0.45-µm or finer pore size and use the filtrate. [Note—Alternatively, centrifuge the solution and use the supernatant.]▲ (IRA 1-Nov-2024)

Reference solution: ▲0.048 mg/mL of fexofenadine hydrochloride and 0.096 mg/mL of pseudoephedrine hydrochloride from the *Sample solution* in *Mobile phase*. Filter the solution before analysis.▲ (IRA 1-Nov-2024)

System suitability

Samples: *System suitability solution*, *Standard solution*, and ▲*Sensitivity solution*▲ (IRA 1-Nov-2024)

▲[Note—The relative retention times in *Table 11* are provided as information that could aid in peak assignment.]

Table 11▲ (IRA 1-Nov-2024)

Name	Relative Retention Time
Pseudoephedrine	1.0
Fexofenadine	1.0
▲Methcathinone[a]▲ (IRA 1-Nov-2024)	1.2[b]
Fexofenadine related compound A	1.2[c]
▲Fexofenadine olefin▲ (IRA 1-Nov-2024) [d]	1.8
▲Fexofenadine related compound C	2.3▲ (IRA 1-Nov-2024) [c]

[a] 2-(Methylamino)-1-phenylpropan-1-one.

[b] Relative to pseudoephedrine.

[c] Relative to fexofenadine.

[d] ▲2-(4-{4-[4-(Diphenylmethylene)piperidin-1-yl]-1-hydroxybutyl}phenyl)-2-methylpropanoic acid.▲ (IRA 1-Nov-2024)

Suitability requirements

Resolution: NLT ▲1.5▲ (IRA 1-Nov-2024) between pseudoephedrine and ▲methcathinone,▲ (IRA 1-Nov-2024) *System suitability solution*; NLT 2.0 between fexofenadine and fexofenadine related compound A, *Standard solution*

Relative standard deviation: NMT 1.0% for ▲▲ (IRA 1-Nov-2024) pseudoephedrine ▲▲ (IRA 1-Nov-2024) , *System suitability solution*; NMT 1.0% for ▲▲ (IRA 1-Nov-2024) fexofenadine;▲▲ (IRA 1-Nov-2024) and NMT 3.0% ▲each▲ (IRA 1-Nov-2024) for fexofenadine related compound A and ▲fexofenadine related compound C,▲ (IRA 1-Nov-2024) *Standard solution*

▲**Signal-to-noise ratio:** NLT 10 for fexofenadine and pseudoephedrine, *Sensitivity solution*▲ (IRA 1-Nov-2024)

Analysis

Samples: ▲*Standard solution*,▲ (IRA 1-Nov-2024) *Sample solution*, and *Reference solution*

Calculate the percentage of fexofenadine related compound A and ▲fexofenadine related compound C▲ (IRA 1-Nov-2024) in the portion of Tablets taken:

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

r_U = ▲▲ (IRA 1-Nov-2024) peak area response of ▲▲ (IRA 1-Nov-2024) fexofenadine related compound A or ▲fexofenadine related compound C▲ (IRA 1-Nov-2024) from the *Sample solution*

r_S = peak area response of fexofenadine related compound A or ▲fexofenadine related compound C▲ (IRA 1-Nov-2024) from the *Standard solution*

C_S = concentration of ▲▲ (IRA 1-Nov-2024) USP Fexofenadine Related Compound A RS or ▲USP Fexofenadine Related Compound C RS▲ (IRA 1-Nov-2024) in the *Standard solution* (mg/mL)

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

Calculate the percentage of ▲methcathinone▲ (IRA 1-Nov-2024) 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 height response of ▲methcathinone▲ (IRA 1-Nov-2024) from the *Sample solution*

r_S = peak height response of pseudoephedrine from the *Standard solution*

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

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

F = relative response factor for ▲methcathinone,▲ (IRA 1-Nov-2024) 0.394

Calculate the percentage of ▲fexofenadine olefin or any unspecified degradation product▲ (IRA 1-Nov-2024) in the portion of Tablets taken:

$$\text{Result} = r_U/(F \times r_S + r_T) \times 100$$

r_U = ▲▲ (IRA 1-Nov-2024) peak area response of ▲fexofenadine olefin or each unspecified degradation product▲ (IRA 1-Nov-2024) from the *Sample solution*

F = difference in concentration between the *Sample solution* and the *Reference solution*, 25

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

r_T = sum of the peak area responses of all ▲unspecified degradation products▲ (IRA 1-Nov-2024) from the *Sample solution*

▲▲ (IRA 1-Nov-2024)

Acceptance criteria: See *Table 12*. ▲Use an appropriate reporting threshold. See *User-Determined Reporting Thresholds ⟨477⟩*. [NOTE—A reporting threshold of 0.1% may be suitable when the maximum daily dose is ≤1g.]▲ (IRA 1-Nov-2024)

Table 12

Name	Acceptance Criteria, NMT (%)
▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)
▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)
▲Methcathinone▲ (IRA 1-Nov-2024)	0.2
Fexofenadine related compound A	0.4
▲Fexofenadine olefin▲ (IRA 1-Nov-2024)	0.2
▲Fexofenadine related compound C▲ (IRA 1-Nov-2024)	0.2
Any ▲unspecified degradation product▲ (IRA 1-Nov-2024)	0.2

Name	Acceptance Criteria, NMT (%)
Total ▲degradation products▲ (IRA 1-Nov-2024)	0.8

Change to read:

• **Organic Impurities, Procedure 2**

Solution A: Dissolve 2.7 g of monobasic potassium phosphate and 2.2 g of sodium 1-octanesulfonate in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.50 ± 0.05.

Mobile phase: Methanol and *Solution A* ▲(60:40)▲ (IRA 1-Nov-2024)

Standard stock solution: 0.18 mg/mL of USP Fexofenadine Hydrochloride RS in *Mobile phase*

Standard solution: 0.0108 mg/mL of USP Fexofenadine Hydrochloride RS▲from the *Standard stock solution*▲ (IRA 1-Nov-2024) in *Mobile phase* ▲▲ (IRA 1-Nov-2024)

Sensitivity solution: ▲1.08▲ (IRA 1-Nov-2024) µg/mL of USP Fexofenadine Hydrochloride RS ▲from the *Standard solution*▲ (IRA 1-Nov-2024) in *Mobile phase* ▲▲ (IRA 1-Nov-2024)

Sample solution: ▲Nominally 1.08 mg/mL of fexofenadine hydrochloride from Tablets prepared as follows.▲ (IRA 1-Nov-2024) Weigh and finely powder 9 Tablets, and quantitatively transfer ▲a suitable amount of▲ (IRA 1-Nov-2024) the ground powder to a ▲suitable▲ (IRA 1-Nov-2024) volumetric flask, with the aid of ▲40% of the flask volume▲ (IRA 1-Nov-2024) of *Mobile phase*. Sonicate for 10 min, and add an additional ▲20% of the flask volume▲ (IRA 1-Nov-2024) of *Mobile phase*. Shake by mechanical means for 30 min, and dilute with *Mobile phase* to volume. Pass a portion of the solution through a polypropylene or polysulfone membrane filter of 0.45-µm pore size, and discard ▲an appropriate volume▲ (IRA 1-Nov-2024) of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 6 times the retention time of fexofenadine▲ (IRA 1-Nov-2024)

System suitability

Samples: *Standard solution* and *Sensitivity solution*

▲[Note—The relative retention times in *Table 13* are provided as information that could aid in peak assignment.]

Table 13▲ (IRA 1-Nov-2024)

Name	Relative Retention Time
Fexofenadine	1.0
▲ Fexofenadine related compound B[a]▲ (IRA 1-Nov-2024)	1.14
Fexofenadine related compound A	1.38
▲Fexofenadine olefin▲ (IRA 1-Nov-2024) [b]	2.25

[a] 2-(3-{1-Hydroxy-4-[4-(hydroxydiphenylmethyl)piperidin-1-yl]butyl}phenyl)-2-methylpropanoic acid.

[b] ▲2-(4-{4-[4-(Diphenylmethylene)piperidin-1-yl]-1-hydroxybutyl}phenyl)-2-methylpropanoic acid.▲ (IRA 1-Nov-2024)

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the amount of each ▲degradation product▲ (IRA 1-Nov-2024) as a percentage of the label claim of fexofenadine hydrochloride 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 response of ▲each degradation product▲ (IRA 1-Nov-2024) 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)

F = relative response factor for each ▲degradation product▲ (IRA 1-Nov-2024) (see ▲*Table 14*▲ (IRA 1-Nov-2024))

Acceptance criteria: See *Table 14*.▲Use an appropriate reporting threshold. See *User-Determined Reporting Thresholds ⟨477⟩*. [NOTE—A reporting threshold of 0.1% may be suitable when the maximum daily dose is ≤1g.]▲ (IRA 1-Nov-2024)

Table 14

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)
▲Fexofenadine related compound B▲ (IRA 1-Nov-2024)	1.0	0.2
Fexofenadine related compound A	0.83	0.4
▲Fexofenadine olefin▲ (IRA 1-Nov-2024)	1.3	0.2
▲Any unspecified degradation product▲ (IRA 1-Nov-2024)	1.0	0.2
Total ▲degradation products▲ (IRA 1-Nov-2024)	—	0.5

Change to read:

• **ORGANIC IMPURITIES, PROCEDURE 3**

Solution A: 4 ▲g/L▲ (IRA 1-Nov-2024) of ammonium acetate

Mobile phase: Methanol and *Solution A* ▲(95:5)▲ (IRA 1-Nov-2024)

Diluent: Methanol and water ▲(50:50)▲ (IRA 1-Nov-2024)

Standard stock solution: 0.18 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Diluent*

Standard solution: 0.0216 mg/mL of USP Pseudoephedrine Hydrochloride RS from the *Standard stock solution* in *Diluent*

Sensitivity solution: ▲2.16▲ (IRA 1-Nov-2024) µg/mL of USP Pseudoephedrine Hydrochloride RS from the *Standard solution* in *Diluent*

Sample solution: ▲Nominally 2.16 mg/mL of pseudoephedrine hydrochloride from Tablets prepared as follows.▲ (IRA 1-Nov-2024) Weigh and finely powder 9 Tablets, and quantitatively transfer ▲a suitable amount of▲ (IRA 1-Nov-2024) the ground powder to a ▲suitable▲ (IRA 1-Nov-2024) volumetric flask, with the aid of ▲40% of the flask volume▲ (IRA 1-Nov-2024) of *Diluent*. Sonicate for 10 min, and add an additional ▲20% of the flask volume▲ (IRA 1-Nov-2024) of *Diluent*. Shake by mechanical means for 30 min, dilute with *Diluent* to volume, and mix. Pass a portion of the solution through a polypropylene or polysulfone membrane filter of 0.45-µm pore size, and discard ▲an appropriate volume▲ (IRA 1-Nov-2024) of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

▲[NOTE—The relative retention times for methcathinone and pseudoephedrine are 0.85 and 1.0, respectively. These relative retention times are provided as information that could aid in peak assignment.]▲ (IRA 1-Nov-2024)

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the amount of ▲any degradation product▲ (IRA 1-Nov-2024) as a percentage of the label claim of pseudoephedrine hydrochloride 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 response of ▲each degradation product▲ (IRA 1-Nov-2024) from the *Sample solution*

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

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

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

F = relative response factor, ▲(see *Table 15*)▲ (IRA 1-Nov-2024)

Acceptance criteria: ▲See *Table 15*. Use an appropriate reporting threshold. See *User-Determined Reporting Thresholds ⟨477⟩*.

[NOTE—A reporting threshold of 0.1% may be suitable when the maximum daily dose is ≤1g.]

Table 15▲ (IRA 1-Nov-2024)

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Methcathinone▲ (IRA 1-Nov-2024)	0.52	0.2
▲Any unspecified degradation product	1.0	0.2▲ (IRA 1-Nov-2024)

Change to read:

• **ORGANIC IMPURITIES, PROCEDURE 4**

Solution A: Dissolve 2.7 g of monobasic potassium phosphate and 2.2 g of sodium 1-octanesulfonate in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.50 ± 0.05.

Solution B: Methanol and *Solution A* ▲(40:60)▲ (IRA 1-Nov-2024)

Solution C: Methanol and *Solution A* ▲(70:30)▲ (IRA 1-Nov-2024)

Mobile phase: See *Table 16*.

Table 16

Time (min)	Solution B (%)	Solution C (%)
0	100	0
40	100	0
41	0	100

Time (min)	Solution B (%)	Solution C (%)
65	0	100
66	100	0
90	100	0

Diluent: Methanol and water ▲(50:50)▲ (IRA 1-Nov-2024)

Standard stock solution: 0.18 mg/mL of USP Benzoic Acid RS in *Diluent*

Standard solution: 0.0216 mg/mL of USP Benzoic Acid RS from the *Standard stock solution* in *Diluent*

Sensitivity solution: 1.08 µg/mL of USP Benzoic Acid RS from the *Standard solution* in *Diluent*

Sample solution: ▲Nominally 2.16 mg/mL of pseudoephedrine hydrochloride from Tablets prepared as follows.▲ (IRA 1-Nov-2024) Weigh and finely powder 9 Tablets, and quantitatively transfer ▲a suitable amount of▲ (IRA 1-Nov-2024) the ground powder to a ▲suitable▲ (IRA 1-Nov-2024) volumetric flask, with the aid of ▲40% of the flask volume▲ (IRA 1-Nov-2024) of *Diluent*. Sonicate for 10 min, and add an additional ▲20% of the flask volume▲ (IRA 1-Nov-2024) of *Diluent*. Shake by mechanical means for 30 min, dilute with *Diluent* to volume, and mix. Pass a portion of the solution through a polypropylene or polysulfone membrane filter of 0.45-µm pore size, and discard ▲an appropriate volume▲ (IRA 1-Nov-2024) of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

▲[NOTE—The relative retention times in *Table 17* are provided as information that could aid in peak assignment.]

Table 17▲ (IRA 1-Nov-2024)

Name	Relative Retention Time
Benzaldehyde	0.43
Benzoic acid	0.55
▲Methcathinone[a]▲ (IRA 1-Nov-2024) [b]	0.97
Pseudoephedrine	1.0

▲[a] 2-(Methylamino)-1-phenylpropan-1-one.▲ (IRA 1-Nov-2024)

[b] ▲Methcathinone▲ (IRA 1-Nov-2024) is not quantitated in this method. A separate method is used for the quantitation of this impurity.

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the amount of ▲any degradation product▲ (IRA 1-Nov-2024) as a percentage of the label claim of pseudoephedrine hydrochloride 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 response of ▲each degradation product▲ (IRA 1-Nov-2024) from the *Sample solution*

r_S = peak response of benzoic acid from the *Standard solution*

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

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

F = relative response factor for each ▲degradation product▲ (IRA 1-Nov-2024) (see *Table 18*)

Acceptance criteria: ▲See *Table 18*. Use an appropriate reporting threshold. See *User-Determined Reporting Thresholds ⟨477⟩*. [NOTE—A reporting threshold of 0.1% may be suitable when the maximum daily dose is ≤1g, for compounds other than benzaldehyde and benzoic acid.]▲ (IRA 1-Nov-2024)

Table 18

Name	Relative Response Factor[a]	Acceptance Criteria, NMT(%)
Benzaldehyde	0.40	0.1
Benzoic acid	1.0	0.1
▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)
▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)	▲▲ (IRA 1-Nov-2024)
▲Any unspecified degradation product▲ (IRA 1-Nov-2024)	0.52[b]	▲0.2▲ (IRA 1-Nov-2024)
Total ▲degradation products▲ (IRA 1-Nov-2024) [c]	▲—▲ (IRA 1-Nov-2024)	0.3

[a] Response factors relative to benzoic acid.

[b] The response factor of pseudoephedrine relative to that of benzoic acid is used in the calculation of ▲any▲ (IRA 1-Nov-2024) unspecified ▲degradation product.▲ (IRA 1-Nov-2024)

[c] Sum of the total ▲degradation products▲ (IRA 1-Nov-2024) from ▲*Organic Impurities*,▲ (IRA 1-Nov-2024) *Procedure 3* and *Procedure 4*.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.

Change to read:

• **LABELING:** ▲▲ (IRA 1-Nov-2024) The labeling states the ▲*Dissolution*▲ (IRA 1-Nov-2024) test used only if *Test 1* is not used. If a test for *Organic Impurities* other than *Procedure 1* is used, the labeling states with which *Procedures* the article complies.

Change to read:

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Benzoic Acid RS

USP Fexofenadine Hydrochloride RS

USP Fexofenadine Related Compound A RS

2-(4-{4-[4-(Hydroxydiphenylmethyl)piperidin-1-yl]butanoyl}phenyl)-2-methylpropanoic acid.

▲▲ (IRA 1-Nov-2024)

$C_{32}H_{37}NO_4$ 499.65

▲ USP Fexofenadine Related Compound C RS

4-[4-(Hydroxydiphenylmethyl)piperidin-1-yl]-1-(4-isopropylphenyl)butan-1-ol hydrochloride.

$C_{31}H_{39}NO_2 \cdot HCl$ 494.12▲ (IRA 1-Nov-2024)

USP Pseudoephedrine Hydrochloride RS

[1] A suitable sinker is available as catalog number CAPWST-31 from www.qla-llc.com.

Topic/Question	Contact	Expert Committee
FEXOFENADINE HYDROCHLORIDE AND PSEUDOEPHEDRINE HYDROCHLORIDE EXTENDED-RELEASE TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

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