

Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Nov-2024
Document Type: USP Monographs
DocId: GUID-921E386F-235F-40B7-8A3E-369E08FDC1F3_7_en-US
DOI: https://doi.org/10.31003/USPNF_M33077_07_01
DOI Ref: 92enu

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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 $\blacktriangle$ (IRA 1-Nov-2024) [USP Fexofenadine Hydrochloride RS](#) and 0.8 mg/mL of $\blacktriangle$ (IRA 1-Nov-2024) [USP Pseudoephedrine Hydrochloride RS](#), $\blacktriangle$ (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*, $\blacktriangle$ (IRA 1-Nov-2024)

Sample stock solution: Nominally $\blacktriangle$ (IRA 1-Nov-2024) 1.2 mg/mL of fexofenadine hydrochloride and 2.4 mg/mL of pseudoephedrine hydrochloride $\blacktriangle$ from Tablets prepared as follows. $\blacktriangle$ (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. $\blacktriangle$ (IRA 1-Nov-2024) Pass a portion of this solution through a filter of 0.45- μ m or finer pore size, and use the filtrate. $\blacktriangle$ [NOTE—Alternatively, centrifuge the *Sample stock solution*, and use the supernatant to prepare the *Sample solution*.] $\blacktriangle$ (IRA 1-Nov-2024)

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

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm $\times$ 5-cm; 5- μ m packing [L6](#) connected in series to a 4.6-mm $\times$ 25-cm; 5- μ m packing [L11](#)

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between pseudoephedrine and $\blacktriangle$ methcathinone, $\blacktriangle$ (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 $\blacktriangle$ (IRA 1-Nov-2024) pseudoephedrine, $\blacktriangle$ *Standard solution*; $\blacktriangle$ (IRA 1-Nov-2024) NMT 1.0% for $\blacktriangle$ (IRA 1-Nov-2024) fexofenadine $\blacktriangle$ (IRA 1-Nov-2024), *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate $\blacktriangle$ (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 $\blacktriangle$ (IRA 1-Nov-2024) fexofenadine or pseudoephedrine from the *Sample solution*

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

C_S = concentration of $\blacktriangle$ (IRA 1-Nov-2024) [USP Fexofenadine Hydrochloride RS](#) or [USP Pseudoephedrine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of $\blacktriangle$ (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* $\blacktriangle$ (65:35) $\blacktriangle$ (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 sinkers¹

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