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Naproxen Sodium and Pseudoephedrine Hydrochloride Extended-Release Tablets

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DEFINITION

Naproxen Sodium and Pseudoephedrine Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

- A.** The retention times of the naproxen and pseudoephedrine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- B.** The UV absorption spectra of the naproxen and pseudoephedrine peaks of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the corresponding peaks of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Buffer: Dissolve 400 mg of [sodium lauryl sulfate](#) in 1 L of [water](#). Add 5 mL of [triethylamine](#) and adjust with [glacial acetic acid](#) to a pH of 4.1.

Mobile phase: [Acetonitrile](#), [methanol](#), and *Buffer* (25:25:50)

Standard solution: 0.22 mg/mL of [USP Naproxen Sodium RS](#) and 0.12 mg/mL of [USP Pseudoephedrine Hydrochloride RS](#) in [methanol](#)

Sample stock solution: Nominally 2.2 mg/mL of naproxen sodium and 1.2 mg/mL of pseudoephedrine hydrochloride in [methanol](#) prepared as follows. Transfer NLT 5 whole Tablets to an appropriate volumetric flask, add 70% of the final volume of [methanol](#), and shake to disintegrate the Tablets. Sonicate for 30 min with intermittent shaking. Allow the solution to cool to room temperature and dilute with [methanol](#) to volume. Centrifuge 10 mL of the solution for 10 min, and use the clear supernatant to prepare the *Sample solution*.

Sample solution: Nominally 0.22 mg/mL of naproxen sodium and 0.12 mg/mL of pseudoephedrine hydrochloride in [methanol](#) from the *Sample stock solution*. Pass a portion of the solution through a suitable filter of 0.45- μ m pore size.

Chromatographic system

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

Mode: LC

Detector: UV 257 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L1](#)

Flow rate: 1.0 mL/min

Injection volume: 10 μ L

Run time: NLT 6 times the retention time of pseudoephedrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for the naproxen and pseudoephedrine peaks

Relative standard deviation: NMT 2.0% for the naproxen and pseudoephedrine peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) 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 naproxen or pseudoephedrine from the *Sample solution*

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

C_S = concentration of [USP Naproxen Sodium RS](#) or [USP Pseudoephedrine Hydrochloride RS](#) in the *Standard solution*, mg/mL

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Medium: 0.01% ▲ [sodium dodecyl sulfate](#) ▲ (RB 1-Sep-2024) in [water](#), degassed; 900 mL

Apparatus 1: 75 rpm

Times

Naproxen sodium: 1 h

Pseudoephedrine hydrochloride: 1, 3, and 8 h

Buffer: Add 5 mL of [triethylamine](#) to 1 L of 0.4 g/L of ▲ [sodium dodecyl sulfate](#) ▲ (RB 1-Sep-2024) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.1.

Mobile phase: [Acetonitrile](#), [methanol](#), and *Buffer* (25:25:50)

Standard stock solution: 1.22 mg/mL of [USP Naproxen Sodium RS](#) and 0.66 mg/mL of [USP Pseudoephedrine Hydrochloride RS](#) in [methanol](#)

Standard solution: 0.24 mg/mL of [USP Naproxen Sodium RS](#) and 0.13 mg/mL of [USP Pseudoephedrine Hydrochloride RS](#) in *Medium* from the *Standard stock solution*

Sample solution: At the times specified, withdraw 10 mL of the solution under test, and pass through a suitable filter of 0.45-μm pore size. Replace the aliquots withdrawn for analysis with equal volumes of fresh portions of *Medium* maintained at 37°.

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 40 μL

Run time: NLT 2.5 times the retention time of pseudoephedrine

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for pseudoephedrine and naproxen are 0.5 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for the naproxen and pseudoephedrine peaks

Relative standard deviation: NMT 2.0% for the naproxen and pseudoephedrine peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) dissolved:

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

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

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

C_S = concentration of [USP Naproxen Sodium RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim of naproxen sodium (mg/Tablet)

Calculate the concentration (C_i), in mg/mL, 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):



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

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

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

- C_i

= concentration of pseudoephedrine hydrochloride in *Medium* in the portion of the sample withdrawn at each time point (*i*) (mg/mL)
- V

= volume of *Medium*, 900 mL
- L

= label claim of pseudoephedrine hydrochloride (mg/Tablet)
- V_s

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

Tolerances

- Naproxen sodium:** NLT 80% (*Q*) of the labeled amount of naproxen sodium ($C_{14}H_{13}NaO_3$) is dissolved.
- Pseudoephedrine hydrochloride:** See [Table 1](#).

Table 1

Time Point (<i>i</i>)	Time (h)	Amount of Pseudoephedrine Hydrochloride Dissolved (%)
1	1	35–55
2	3	75–95
3	8	NLT 85

The percentages of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) 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 it meets USP *Dissolution Test 2*.

- Medium:** 0.01% ▲ [sodium dodecyl sulfate](#) ▲ (RB 1-Sep-2024) in [water](#); 900 mL
- Apparatus 1:** 75 rpm
- Times**

Naproxen sodium: 1 h

Pseudoephedrine hydrochloride: 1, 3, and 8 h
- Solution A:** Dissolve 6.8 g of [monobasic potassium phosphate](#) in 1 L of [water](#). Adjust with [phosphoric acid](#) to a pH of 4.0.
- Solution B:** [Acetonitrile](#)
- Mobile phase:** See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
10.0	45	55
11.0	90	10
14.0	90	10

- Standard solution:** 0.24 mg/mL of [USP Naproxen Sodium RS](#) and 0.13 mg/mL of [USP Pseudoephedrine Hydrochloride RS](#) prepared as follows. Dissolve suitable quantities of [USP Naproxen Sodium RS](#) and [USP Pseudoephedrine Hydrochloride RS](#) with 2% of the final volume of [methanol](#) and sonicate if necessary. Dilute with *Medium* to volume.
- Sample solution:** At the times specified, withdraw 10 mL of the solution under test, and pass through a suitable filter of 0.45-µm pore size.
- Chromatographic system**

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

Mode: LC