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Buprenorphine and Naloxone Sublingual Tablets

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DEFINITION

Buprenorphine and Naloxone Sublingual Tablets contain amounts of buprenorphine hydrochloride and naloxone hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of buprenorphine (C₂₉H₄₁NO₄) and naloxone (C₁₉H₂₁NO₄).

IDENTIFICATION

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

ASSAY

• **PROCEDURE**

[NOTE—It is suggested to protect all solutions containing buprenorphine and naloxone from light.]

Buffer: 9 mM of [dibasic ammonium phosphate](#) in [water](#). Adjust with a solution of [phosphoric acid](#) and [water](#) (1:1) to a pH of 6.2.

Solution A: [Acetonitrile](#), [methanol](#), and *Buffer* (7:3:90)

Solution B: [Acetonitrile](#), [methanol](#), and *Buffer* (56:24:20)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	99	1
30	1	99
45	1	99
45.1	99	1
55	99	1

Solution C: [Phosphoric acid](#) and [water](#) (1:1000)

Diluent: [Acetonitrile](#), [methanol](#), and *Solution C* (7:3:90)

Standard solution: 0.57 mg/mL of [USP Buprenorphine Hydrochloride RS](#) and 0.13 mg/mL of [USP Naloxone RS](#) in *Diluent*

Sample solution: Nominally 0.52 mg/mL of buprenorphine and 0.13 mg/mL of naloxone prepared as follows. Transfer NLT 13 Tablets to a suitable volumetric flask, and add about 70% of the final volume of *Diluent*. Sonicate for 15 min with occasional swirling and shake for 15 min. Dilute with *Diluent* to volume. Pass a portion through a suitable filter of 0.45-µm pore size. Discard the first 5 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing [L11](#)

Column temperature: 60°

Flow rate: 0.8 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both buprenorphine and naloxone

Relative standard deviation: NMT 2.0% for both buprenorphine and naloxone

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of buprenorphine ($C_{29}H_{41}NO_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of buprenorphine, 467.65

M_{r2} = molecular weight of buprenorphine hydrochloride, 504.11

Calculate the percentage of the labeled amount of naloxone ($C_{19}H_{21}NO_4$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0% of the labeled amount of buprenorphine ($C_{29}H_{41}NO_4$) and naloxone ($C_{19}H_{21}NO_4$)

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

▲Test 1▲ (RB 1-Nov-2024)

Medium: [Water](#) (deaerated for 5 min); 500 mL

Apparatus 1: 100 rpm

Time: 10 min

Buffer: 0.018 M monobasic potassium phosphate in [water](#) prepared as follows. Dissolve 2.4 g of [monobasic potassium phosphate](#) and 0.5 g of [sodium hydroxide](#) in each liter of [water](#). Adjust with [phosphoric acid](#) to a pH of 6.8.

Solution A: [Acetonitrile](#), [methanol](#), and *Buffer* (40:20:40)

Solution B: [Acetonitrile](#) and *Buffer* (78:22)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
2.0	100	0
3.0	0	100
6.0	0	100
6.1	100	0
8.0	100	0

Diluent: [Methanol](#) and [water](#) (50:50)

Standard solution: 0.01 mg/mL of [USP Buprenorphine Hydrochloride RS](#) and 0.0025 mg/mL of [USP Naloxone RS](#) in *Diluent*. Sonicate if necessary. Pass a portion through a suitable filter of 0.45-μm pore size. Discard the first 4 mL of filtrate.

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 230 nm

Column: 4.6-mm × 5-cm; 5-μm packing [L7](#)

Column temperature: 25°

Flow rate: 1.0 mL/min

Injection volume: 40 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both buprenorphine and naloxone

Relative standard deviation: NMT 2.0% for both buprenorphine and naloxone

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of buprenorphine ($C_{29}H_{41}NO_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 500 mL

M_{r1} = molecular weight of buprenorphine, 467.65

M_{r2} = molecular weight of buprenorphine hydrochloride, 504.11

L = label claim of buprenorphine (mg/Tablet)

Calculate the percentage of the labeled amount of naloxone ($C_{19}H_{21}NO_4$) dissolved:

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

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

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

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

V = volume of *Medium*, 500 mL

L = label claim of naloxone (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of buprenorphine ($C_{29}H_{41}NO_4$) and naloxone ($C_{19}H_{21}NO_4$) is dissolved.

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

Medium: [Water](#); 500 mL

Apparatus 1: 100 rpm

Time: 8 min

Solution A: 5 mL of [phosphoric acid](#) diluted with [water](#) to 10 mL

Solution B: Dissolve 1.0 g of [sodium chloride](#) and 0.2 g of [octanesulfonic acid sodium salt](#) in 1 L of [water](#). Adjust with *Solution A* to a pH of 2.8.

Solution C: [Methanol](#)

Mobile phase: See [Table 3](#).

Table 3