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Butorphanol Tartrate Nasal Spray

DEFINITION

Butorphanol Tartrate Nasal Spray is an aqueous solution of butorphanol tartrate for administration as a metered spray to the nasal mucosa. It contains the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of butorphanol tartrate ($C_{21}H_{29}NO_2 \cdot C_4H_6O_6$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** [THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST \(201\)](#).

Standard solution: 1.0 mg/mL of [USP Butorphanol Tartrate RS](#) in methanol

Sample solution: Prepare a composite solution by pooling the contents of three containers of Nasal Spray into a suitable vessel. Transfer 1.0 mL of pooled sample to a 10-mL volumetric flask, and dilute with methanol to volume.

Developing solvent system: Chloroform, methanol, benzene, and ammonium hydroxide (17:5:4:1)

[**CAUTION**—Prepare in a hood while wearing appropriate safety gloves, lab coat, and protective eyewear.]

Spray reagent: Prepare a 1-in-10 solution of chloroplatinic acid in water. To 0.5 mL of this solution, add 33 mL of water and 1 g of potassium iodide. Prepare fresh daily.

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter, except spray the plate with *Spray reagent*.

Acceptance criteria: The typical R_f value is 0.7 for butorphanol tartrate.

ASSAY

PROCEDURE

Buffer: 3.4 g/L of 0.025 M monobasic potassium phosphate. Filter.

Mobile phase: Acetonitrile, triethylamine, and *Buffer* (15:2:85). Mix thoroughly, and adjust with 85.0% phosphoric acid to a pH of 3.0 ± 0.1 .

Standard solution: 0.2 mg/mL of [USP Butorphanol Tartrate RS](#) in *Mobile phase*. Mix, and filter, discarding the first 2 mL of the filtrate. The *Standard solution* is stable for at least 108 h.

Sample solution: Nominally 0.2 mg/mL of butorphanol tartrate in *Mobile phase* prepared as follows. Prepare a composite solution by pooling a minimum of four containers of Nasal Spray into a suitable glass vessel. Transfer the equivalent of 20 mg of butorphanol tartrate to a 100-mL volumetric flask. Dilute with *Mobile phase* to volume, mix, and filter, discarding the first 2 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Columns

Analytical: 4.6-mm $\times$ 15-cm; 5- μ m packing L11

Guard: 4.6-mm $\times$ 1-cm; 5- μ m packing L11

Column temperature: 30°

Flow rate: 2.0 mL/min

Injection volume: 20 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of butorphanol tartrate ($C_{21}H_{29}NO_2 \cdot C_4H_6O_6$) in the portion of Nasal Spray taken:

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

r_U = peak response from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Butorphanol Tartrate RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of butorphanol tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• ORGANIC IMPURITIES

Buffer: Prepare as directed in the Assay.

Mobile phase: Acetonitrile, triethylamine, and *Buffer* (15:5.1:85). Mix thoroughly, and adjust with 85.0% phosphoric acid to a pH of 3.0 ± 0.1 .

Standard solution: 0.005 mg/mL of [USP Butorphanol Tartrate RS](#)

Sensitivity solution: Transfer 2.5 mL of the *Standard solution* to a 50-mL volumetric flask, and dilute with water to volume. Do not filter.

Sample solution: Nominally 1 mg/mL of butorphanol tartrate in water prepared as follows. Prepare a composite solution by pooling a minimum of four containers of Nasal Spray into a suitable glass vessel. Transfer the equivalent of 50 mg of butorphanol tartrate to a 50-mL volumetric flask. Dilute with water to volume. Do not filter.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Columns

Analytical: 4.6-mm $\times$ 25-cm; 5- μ m packing L11

Guard: 4.6-mm $\times$ 1-cm; 5- μ m packing L11

Column temperature: 40°

Flow rate: 2.0 mL/min

Injection volume: 60 μ L

Run time: 40 min

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 10.0%, *Standard solution*

Sensitivity: The peak height for butorphanol tartrate is greater than or equal to three times the baseline noise, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Record the chromatograms, and measure the responses for the butorphanol tartrate peak in the *Standard solution*, and for all known and unknown related compounds in the *Sample solution*.

Calculate the percentage of each related compound (see [Table 1](#)) and each unknown impurity in the portion of Nasal Spray taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = peak response of each known or unknown related compound from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Butorphanol Tartrate RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of butorphanol tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
3,14-Dihydroxymorphinan	0.3	0.3
Δ 6-Butorphanol	0.7	0.5
Butorphanol tartrate	1.0	—
Unknown impurity	—	—