Dissolve the *Dextrose, Sodium Citrate Anhydrous,* and *Citric Acid Monohydrate* in 5 mL of *Purified Water* in a suitable calibrated container. Add the *Buprenorphine hydrochloride* powder into the mixture and add sufficient *Purified Water* to bring to final volume, and mix well.

ASSAY

- **PROCEDURE**

Mobile phase: Acetonitrile and 10 mM ammonium acetate (80:20)

Standard solution: 0.3 mg/mL of buprenorphine prepared from USP Buprenorphine Hydrochloride RS in methanol

Sample solution: Transfer 1 mL of Buccal Solution, Veterinary into a 10-mL volumetric flask, dilute with methanol to volume, and mix well.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 2.1-mm × 5-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 0.25 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for buprenorphine is about 5.8 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

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 Buccal Solution, Veterinary taken:

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

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

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

C_S = concentration of buprenorphine in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

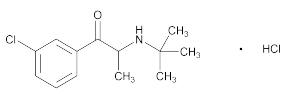
- **pH** ⟨**791**⟩**:** 3.5–4.5

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store at 2°–8°.
- **LABELING:** Label it to indicate that it is for veterinary use only. Label to indicate that it is for buccal administration, and to state the *Beyond-Use Date*.
- **BEYOND-USE DATE:** NMT 90 days after the date on which it was compounded when stored at 2°–8°
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Buprenorphine Hydrochloride RS

Bupropion Hydrochloride



$C_{13}H_{18}ClNO \cdot HCl$ 276.20

1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl) amino]-, hydrochloride, (±)-;

(±)-2-(*tert*-Butylamino)-3′-chloropropiophenone hydrochloride [31677-93-7].

DEFINITION

Bupropion Hydrochloride contains NLT 98.0% and NMT 102.0% of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. IDENTIFICATION TESTS—GENERAL,** *Chloride* ⟨**191**⟩

Sample solution: 1 mg/mL of Bupropion Hydrochloride

Acceptance criteria: Meets the requirements for the silver nitrate precipitate test

ASSAY

- **PROCEDURE**

Diluent: Methanol and water (50:50)

Buffer: 3.4 g/L of monobasic potassium phosphate in water. Adjust with 1 N sodium hydroxide to a pH of 7.0.

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (39:11:50)

Standard solution: 1 mg/mL of USP Bupropion Hydrochloride RS and 2 µg/mL each of USP Bupropion Hydrochloride Related Compound A RS and USP Bupropion Hydrochloride Related Compound B RS in *Diluent*

Sample solution: 1 mg/mL of Bupropion Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 3.9-mm × 15-cm; 5-µm packing L7

Flow rate: 1.1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between bupropion hydrochloride related compound A and bupropion; NLT 1.3 between bupropion and bupropion hydrochloride related compound B

Relative standard deviation: NMT 2.0% for bupropion

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the portion of Bupropion Hydrochloride 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 Bupropion Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Bupropion Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **LIMIT OF 3-CHLOROBENZOIC ACID**

Protect all analytical solutions from light and use within one day.

Diluent: Methanol and 0.001 N hydrochloric acid (20:80)

Solution A: Acetonitrile and water (10:90). Add 0.4 mL of trifluoroacetic acid per L of the mixture.
Solution B: Acetonitrile and water (95:5). Add 0.3 mL of trifluoroacetic acid per L of the mixture.
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3.4	87	13
10.0	15	85
10.1	0	100
13.0	0	100
13.2	90	10
19.0	90	10

System suitability stock solution: 0.02 mg/mL of USP Bupropion Hydrochloride Related Compound C RS, 0.02 mg/mL of USP Bupropion Hydrochloride Related Compound F RS, and 0.012 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol
System suitability solution: 0.002 mg/mL of bupropion hydrochloride related compound C, 0.002 mg/mL of bupropion hydrochloride related compound F, and 0.0012 mg/mL of 3-chlorobenzoic acid from *System suitability stock solution* in *Diluent*
Standard stock solution: 0.06 mg/mL of USP 3-Chlorobenzoic Acid RS in methanol
Standard solution: 1.2 µg/mL of USP 3-Chlorobenzoic Acid RS from *Standard stock solution* in *Diluent*
Sample solution: 600 µg/mL of Bupropion Hydrochloride in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 226 nm
Column: 4.6-mm × 10-cm; 3.5-µm packing L1
Column temperature: 40°
Flow rate: 1.5 mL/min
Injection volume: 5 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—See *Table 2* for the relative retention times.]
Suitability requirements
Resolution: NLT 1.3 between bupropion hydrochloride related compound F and bupropion hydrochloride related compound C, *System suitability solution*; NLT 1.5 between bupropion hydrochloride related compound C and 3-chlorobenzoic acid, *System suitability solution*
Relative standard deviation: NMT 5.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of 3-chlorobenzoic acid in the portion of Bupropion Hydrochloride taken:

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

r_U = peak response of 3-chlorobenzoic acid from the *Sample solution*
r_S = peak response of 3-chlorobenzoic acid from the *Standard solution*
C_S = concentration of USP 3-Chlorobenzoic Acid RS in the *Standard solution* (µg/mL)
C_U = concentration of Bupropion Hydrochloride in the *Sample solution* (µg/mL)
Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Bupropion	1.0	—
Bupropion hydrochloride related compound F[a]	1.71	—
Bupropion hydrochloride related compound C[a]	1.75	—
3-Chlorobenzoic acid	1.80	0.2

[a] Included for system suitability purposes only.

• **ORGANIC IMPURITIES**
Diluent, Buffer, Mobile phase, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
System suitability
Sample: *Standard solution*
[NOTE—See *Table 3* for the relative retention times.]
Suitability requirements
Resolution: NLT 1.3 between bupropion hydrochloride related compound A and bupropion; NLT 1.3 between bupropion and bupropion hydrochloride related compound B
Relative standard deviation: NMT 2.0% for bupropion; NMT 5.0% for bupropion hydrochloride related compound B
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Bupropion Hydrochloride taken:

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

r_U = peak response for each impurity from the *Sample solution*
r_S = peak response for bupropion from the *Standard solution*
C_S = concentration of USP Bupropion Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = concentration of Bupropion Hydrochloride in the *Sample solution* (mg/mL)
F = relative response factor for each impurity relative to bupropion (see *Table 3*)
Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Deschloro bupropion[a]	0.38	1.5	0.5
Bupropion dione derivative[b]	0.58	1.0	0.2
o-Bupropion[c]	0.71	0.45	0.1
Chloropropiophenone[d]	0.78	1.2	0.1

[a] 2-(*tert*-Butylamino)-1-phenylpropan-1-one; also known as 2-(*tert*-butylamino)propiophenone.
[b] 1-(3-Chlorophenyl)propane-1,2-dione; also known as 1-(3-chlorophenyl)-1,2-propanedione.
[c] 2-(*tert*-Butylamino)-1-(2-chlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-2′-chloropropiophenone.
[d] 1-(3-Chlorophenyl)propan-1-one; also known as 3′-chloropropiophenone.
[e] 2-Bromo-1-(3-chlorophenyl)propan-1-one; also known as 2-bromo-3′-chloropropiophenone.
[f] 2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3′,4′-dichloropropiophenone.
[g] 2-(*tert*-Butylamino)-1-(3,5-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3′,5′-dichloropropiophenone.
[h] Sum of all impurities found in the tests for *Limit of 3-Chlorobenzoic Acid* and *Organic Impurities*.

Table 3 *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Bupropion hydrochloride related compound A	0.92	1.4	0.2
Bupropion	1.0	—	—
Bupropion hydrochloride related compound B	1.14	0.81	0.2
Bromochloropropion-phenone[e]	1.63	0.88	0.1
4-Chlorobupropion[f]	2.30	1.1	0.2
5-Chlorobupropion[g]	2.74	0.69	0.2
Any individual impurity	—	1.0	0.1
Total impurities[h]	—	—	1.0

[a] 2-(*tert*-Butylamino)-1-phenylpropan-1-one; also known as 2-(*tert*-butylamino)propiophenone.

[b] 1-(3-Chlorophenyl)propane-1,2-dione; also known as 1-(3-chlorophenyl)-1,2-propanedione.

[c] 2-(*tert*-Butylamino)-1-(2-chlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-2′-chloropropiophenone.

[d] 1-(3-Chlorophenyl)propan-1-one; also known as 3′-chloropropiophenone.

[e] 2-Bromo-1-(3-chlorophenyl)propan-1-one; also known as 2-bromo-3′-chloropropiophenone.

[f] 2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3′,4′-dichloropropiophenone.

[g] 2-(*tert*-Butylamino)-1-(3,5-dichlorophenyl)propan-1-one; also known as 2-(*tert*-butylamino)-3′,5′-dichloropropiophenone.

[h] Sum of all impurities found in the tests for *Limit of 3-Chlorobenzoic Acid* and *Organic Impurities*.

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Bupropion Hydrochloride RS
  USP Bupropion Hydrochloride Related Compound A RS
  2-(*tert*-Butylamino)-4′-chloropropiophenone hydrochloride.
  $C_{13}H_{18}ClNO \cdot HCl$ 276.20
  USP Bupropion Hydrochloride Related Compound B RS
  2-(*tert*-Butylamino)-3′-bromopropiophenone hydrochloride.
  $C_{13}H_{18}BrNO \cdot HCl$ 320.66
  USP Bupropion Hydrochloride Related Compound C RS
  1-(3-Chlorophenyl)-2-hydroxypropan-1-one.
  $C_9H_9O_2Cl$ 184.62
  USP Bupropion Hydrochloride Related Compound F RS
  1-(3-Chlorophenyl)-1-hydroxypropan-2-one.
  $C_9H_9O_2Cl$ 184.62
  USP 3-Chlorobenzoic Acid RS
  3-Chlorobenzoic acid.
  $C_7H_5ClO_2$ 156.57

Bupropion Hydrochloride Tablets

DEFINITION

Bupropion Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$).

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
  Sample: Crush 1 Tablet using a mortar and pestle. Prepare an approximate 1% (w/w) dispersion of the sample in potassium bromide.
  Acceptance criteria: The *Sample* shows strong bands at about 1690, 1560, and 1240 cm^{-1} and a weaker band at about 740 cm^{-1}, similar to the reference preparation.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay.*

ASSAY

- **PROCEDURE**
  Buffer: 6.8 g/L of monobasic potassium phosphate and 1.164 g/L of sodium hydroxide in water
  Mobile phase: Methanol and *Buffer* (65:35)
  Diluent: Methanol and water (65:35)
  Standard solution: 0.6 mg/mL of USP Bupropion Hydrochloride RS in *Diluent*
  Sample stock solution: Nominally 3.0 mg/mL of bupropion hydrochloride in *Diluent* prepared as follows. Transfer an appropriate number of Tablets to a suitable volumetric flask. Add 50% of the flask volume of *Diluent*, and shake by mechanical means until the Tablets have disintegrated (30–60 min). Sonicate for 5 min, dilute with *Diluent* to volume, and mix. Allow to stand for at least 30 min. Use the supernatant.
  Sample solution: Nominally 0.6 mg/mL of bupropion hydrochloride from the *Sample stock solution* in *Diluent*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 224 nm
  Column: 4.6-mm × 15-cm; 5-µm base-deactivated packing L1
  Flow rate: 1.2 mL/min
  Injection volume: 10 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 2.5
  Relative standard deviation: NMT 2.0%
  Analysis
  Calculate the percentage of the labeled amount of bupropion hydrochloride ($C_{13}H_{18}ClNO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak area from the *Sample solution*
r_S = peak area from the *Standard solution*
C_S = concentration of USP Bupropion Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of bupropion hydrochloride in the *Sample solution* (mg/mL)

  Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨**711**⟩
  Medium: Water; 900 mL
  Apparatus 2: 50 rpm
  Time: 45 min
  Standard solution: USP Bupropion Hydrochloride RS at a known concentration in 0.1 N hydrochloric acid
  Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with 0.1 N hydrochloric acid, if necessary.