• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements
Procedure for content uniformity
Standard solution: 0.33 mg/mL of USP Bupropion Hydrochloride RS in water
Sample solution: Transfer 1 Tablet to a suitable homogenizer vessel containing a volume of water to obtain a concentration of about 0.33 mg of bupropion hydrochloride per mL. Immediately homogenize the sample using single 30-s pulses each at 5000, 10,000, and 15,000 rpm, and follow by two pulses each at 20,000 rpm. After the homogenate has settled, mix at 5000 rpm for an additional 30 s. Pass a portion of the solution through a nylon filter of 0.45-µm pore size, discarding the first 4 mL of the filtrate.
Analysis: Proceed as directed for the appropriate *Dissolution* procedure, using a 0.5-cm cell, and correct for dilution.

IMPURITIES

• **ORGANIC IMPURITIES**
Solution A, Solution B, Mobile phase, System suitability solution A, System suitability solution B, Standard solution, Sample solution A or **Sample solution B**, and **Chromatographic system:** Proceed as directed in the *Assay*.
Analysis
Samples: *Standard solution* and *Sample solution A* or *Sample solution B*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each impurity from *Sample solution A* or *Sample solution B*
r_S = peak response of bupropion hydrochloride 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 *Sample solution A* or *Sample solution B* (mg/mL)
F = relative response factor for each impurity (see *Table 11* for values)
Acceptance criteria: See *Table 11*.

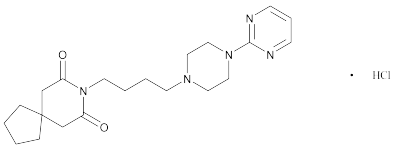
Table 11

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%) 100 mg or less	Acceptance Criteria, NMT (%) 150 mg or greater
2-Amino-1-(3-chlorophenyl)-1-propanone	0.38	0.80	0.3	0.3
(3*S*,5*S*,6*S*)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid	0.56	0.86	1.0	1.5
(3*S*,5*R*,6*R*)-6-(3-Chlorophenyl)-6-hydroxy-5-methyl-3-thiomorpholine carboxylic acid	0.78	0.88	0.5	0.4
Bupropion	1.0	—	—	—
Bupropion related compound F	1.71	0.55	1.2	2.3
Bupropion related compound C	1.75	0.59	0.3	0.3
m-Chlorobenzoic acid	1.80	0.24	0.3	0.3
1-(3-Chlorophenyl)-1,2-propanedione	2.25	1.00	0.4	0.4
Any unspecified impurity	—	1.00	0.2	0.2
Total impurities	—	—	3.2	3.3

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.
• **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
• **USP REFERENCE STANDARDS ⟨11⟩**
USP Bupropion Hydrochloride RS
USP Bupropion Hydrochloride Related Compound C RS
1-(3-Chlorophenyl)-2-hydroxy-1-propanone.
$C_9H_9O_2Cl$ 184.62
USP Bupropion Hydrochloride Related Compound F RS
1-(3-Chlorophenyl)-1-hydroxy-2-propanone.
$C_9H_9O_2Cl$ 184.62

Buspirone Hydrochloride



$C_{21}H_{31}N_5O_2 \cdot HCl$ 421.96
8-Azaspiro[4,5]decane-7,9-dione, 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-, monohydrochloride;
N-[4-[4-(2-Pyrimidinyl)-1-piperazinyl]butyl]-1,1-cyclopentanediacetamide monohydrochloride [33386-08-2; 36505-84-7].

DEFINITION

Buspirone Hydrochloride contains NLT 97.5% and NMT 102.5% of $C_{21}H_{31}N_5O_2 \cdot HCl$, calculated on the as-is basis.

IDENTIFICATION

• **A. INFRARED ABSORPTION ⟨197K⟩**
• **B.** The relative 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⟩:** Meets the requirements

Sample solution: 10 mg/mL in water

ASSAY

- **PROCEDURE**

Buffer: 1.36 g/L of monobasic potassium phosphate in water. Adjust the solution with 10% sodium hydroxide (w/v) to a pH of 7.5, and filter.
Mobile phase: Acetonitrile and *Buffer* (2:3)
Internal standard stock solution: 2.5 mg/mL of propylparaben in methanol
Internal standard solution: 0.125 mg/mL of propylparaben from the *Internal standard stock solution* in water
Standard stock solution: Dissolve 50 mg of USP Buspirone Hydrochloride RS in 25 mL of 1 N hydrochloric acid in a 100-mL volumetric flask, and dilute with water to volume.
Standard solution: To 10.0 mL of *Standard stock solution* in a 50.0-mL volumetric flask add 10.0 mL of *Internal standard solution*, and dilute with water to volume.
Sample stock solution: Dissolve 50 mg of Buspirone Hydrochloride in 25 mL of 1 N hydrochloric acid in a 100-mL volumetric flask, and dilute with water to volume.
Sample solution: 0.1 mg/mL of Buspirone Hydrochloride from the *Sample stock solution* and 0.025 mg/mL of propylparaben from the *Internal standard solution* in water
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 3.9-mm × 30-cm; packing L1
Flow rate: 2 mL/min
Injection size: 25 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for propylparaben and buspirone hydrochloride are about 0.55 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 4 between buspirone hydrochloride and the internal standard
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{21}H_{31}N_5O_2 \cdot HCl$ in the portion of Buspirone Hydrochloride taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of buspirone hydrochloride to propylparaben from the *Sample solution*
R_S = peak response ratio of buspirone hydrochloride to propylparaben from the *Standard solution*
C_S = concentration of USP Buspirone Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = concentration of Buspirone Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 97.5%–102.5% on the as-is basis

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.5%
- **HEAVY METALS,** *Method II* **⟨231⟩:** NMT 20 ppm

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**
USP Buspirone Hydrochloride RS

Buspirone Hydrochloride Tablets

» Buspirone Hydrochloride Tablets contain not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$).

Packaging and storage—Preserve in tight, light-resistant containers, at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Buspirone Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩—

Test specimen—Grind 20 Tablets to a fine powder, add 50 mL of chloroform, stir for 3 to 5 minutes, and filter into a 250-mL evaporating flask. Evaporate the solution with the aid of a rotary evaporator to dryness at low heat. Use the residue.

B: The relative retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩**—**

Medium: 0.01 N hydrochloric acid; 500 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{21}H_{31}N_5O_2$.HCl dissolved by employing UV absorption at the wavelength of maximum absorbances at about 235 nm on filtered portions of the solution under test, suitably diluted with 0.01 N hydrochloric acid, in comparison with a Standard solution having a known concentration of USP Buspirone Hydrochloride RS in the same *Medium*.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{21}H_{31}N_5O_2$.HCl is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Buffer solution, Mobile phase, Internal standard solution, Standard stock solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Buspirone Hydrochloride*.

Assay preparation—Transfer a number of Tablets, equivalent to about 100 mg of buspirone hydrochloride, to a 200-mL volumetric flask, add 50 mL of 1 N hydrochloric acid, and shake for 15 minutes. Add about 100 mL of water, and shake for 30 minutes. Dilute with water to volume, mix, and filter, discarding the first 20 mL of the filtrate. Pipet 10.0 mL of the filtrate and 10.0 mL of *Internal standard solution* into a 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Buspirone Hydrochloride*. Calculate the quantity, in mg, of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$) in the Tablets taken by the formula:

$$(L / D)C(R_U / R_S)$$

in which L is the labeled amount, in mg, of buspirone hydrochloride in each Tablet; D is the concentration, in mg per mL, of buspirone hydrochloride in the *Assay preparation*, based on the labeled quantity per Tablet and the extent of dilution; C is the concentration, in mg per mL, of USP Buspirone Hydrochloride RS in the *Standard preparation;* and R_U and R_S are the peak response ratios of buspirone hydrochloride to propylparaben obtained from the *Assay preparation* and the *Standard preparation,* respectively.