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

PROCEDURE FOR CONTENT UNIFORMITY—

Dye solution—Dissolve 100 mg of bromocresol purple in 1000 mL of 0.33 N acetic acid, and mix.

Acetous methanol—Dilute 100 mL of methanol with sufficient 0.33 N acetic acid to prepare 1000 mL of solution, and mix.

Standard preparation—Transfer about 27 mg of USP Clemastine Fumarate RS, accurately weighed, to a 100-mL volumetric flask, dissolve in 10 mL of methanol, dilute with 0.33 N acetic acid to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with *Acetous methanol* to volume, and mix.

Test preparation—Mix 1 finely powdered Tablet with an accurately measured volume of *Acetous methanol*, sufficient to obtain a solution having a concentration of about 27 µg of clemastine fumarate per mL. Shake for 30 minutes, and filter, discarding the first few mL of the filtrate.

Procedure—Transfer 15.0 mL each of the *Standard preparation*, the *Test preparation*, and *Acetous methanol* to provide the blank to individual 125-mL separators. Add 25 mL of *Dye solution* and 50.0 mL of chloroform to each, and shake by mechanical means for 15 minutes. Allow the layers to separate, and filter the chloroform layers. Concomitantly determine the absorbances of the filtered solutions obtained from the *Test preparation* and the *Standard preparation* at the wavelength of maximum absorbance at about 406 nm, using the blank to set the instrument. Calculate the quantity, in mg, of $C_{21}H_{26}ClNO \cdot C_4H_4O_4$ in the Tablet taken by the formula:

$$(TC / D)(A_U / A_S)$$

in which T is the labeled quantity, in mg, of clemastine fumarate in the Tablet; C is the concentration, in µg per mL, of USP Clemastine Fumarate RS in the *Standard preparation; D* is the concentration, in µg per mL, of clemastine fumarate in the *Test preparation*, based on the labeled quantity per Tablet and the extent of dilution; and A_U and A_S are the absorbances of the solutions from the *Test preparation* and the *Standard preparation*, respectively.

Assay—

pH 7 phosphate buffer—Transfer 9.47 g of anhydrous dibasic sodium phosphate to a 1000-mL volumetric flask, dilute with water to volume, and mix *(flask A)*. Transfer 9.08 g of monobasic potassium phosphate to a 1000-mL volumetric flask, dilute with water to volume, and mix *(flask B)*. Mix 612 mL of *A* with 388 mL of *B*.

Dilute phosphate buffer—Prepare a mixture of 1 volume of *pH 7 phosphate buffer* and 3 volumes of water.

Mobile phase—Prepare a suitable and degassed solution of methanol and *Dilute phosphate buffer* (83:17).

Standard preparation—Dissolve an accurately weighed quantity of USP Clemastine Fumarate RS in a mixture of methanol and water (1:1) to obtain a solution having a known concentration of about 0.14 mg per mL.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 14 mg of clemastine fumarate, to a 200-mL conical flask. Pipet 100 mL of a mixture of methanol and water (1:1) into the flask, shake for 30 minutes, centrifuge, and filter the supernatant.

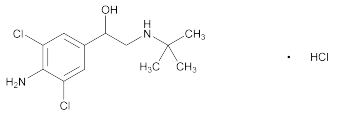
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The flow rate is about 4 mL per minute. Chromatograph five replicate injections of the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 1.5%.

Procedure—Separately inject equal volumes (about 100 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{21}H_{26}ClNO \cdot C_4H_4O_4$ in the portion of Tablets taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Clemastine Fumarate RS in the *Standard preparation*; and r_U and r_S are the peak responses of clemastine fumarate obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Clenbuterol Hydrochloride



$C_{12}H_{18}Cl_2N_2O \cdot HCl$ 313.65

Ethanol, 1-(4-amino-3,5-dichlorophenyl)-2-(*tert*-butylamino), hydrochloride;

4-Amino-α-[(*tert*-butylamino)methyl]-3,5-dichlorobenzyl alcohol, hydrochloride [21898-19-1].

DEFINITION

Clenbuterol Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{12}H_{18}Cl_2N_2O \cdot HCl$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
  [NOTE—Alternatively, *Infrared Absorption* ⟨197A⟩ may be used.]
- **B. Identification Tests—General,** *Chloride* ⟨191⟩**:** Meets the requirements

ASSAY

- **Procedure**
  Sample solution: Dissolve 0.25 g in 50 mL of alcohol, and add 5.0 mL of 0.01 N hydrochloric acid.
  Analysis: Titrate with 0.1 N sodium hydroxide VS, determining the endpoint potentiometrically. Read the volume added between the two points of inflection. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N sodium hydroxide is equivalent to 31.37 mg of $C_{12}H_{18}Cl_2N_2O \cdot HCl$.
  Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%, from 1–2 g
- **Heavy Metals,** *Method II* ⟨231⟩**:** NMT 10 ppm

Organic Impurities

- **Procedure**
  Buffer: Dissolve 3.0 g of sodium 1-decanesulfonate and 5.0 g of monobasic potassium phosphate in 900 mL of water, adjust with dilute phosphoric acid (1 in 10) to a pH of 3.0, and dilute with water to 1000 mL.
  Mobile phase: Acetonitrile, methanol, and *Buffer* (2:2:6)
  System suitability solution: 0.2 mg/mL each of USP Clenbuterol Related Compound B RS and Clenbuterol Hydrochloride in *Mobile phase*
  Sample solution 1: 2.0 mg/mL of Clenbuterol Hydrochloride in *Mobile phase*
  Sample solution 2: 2.0 µg/mL of Clenbuterol Hydrochloride in *Mobile phase*, from *Sample solution 1*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC
Detector: UV 215 nm
Column: 4.0-mm × 12.5-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 0.5 mL/min
Injection size: 5 µL

System suitability
Sample: *System suitability solution*
Suitability requirements
Resolution: NLT 4.0 between clenbuterol related compound B and clenbuterol
Relative standard deviation: NMT 2.0% for the clenbuterol peak

Analysis
Samples: *Sample solution 1* and *Sample solution 2*
Calculate the percentage of impurities in the portion of $C_{12}H_{18}Cl_2N_2O \cdot HCl$ taken:

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

r_U = peak response of each impurity from *Sample solution 1*
r_S = peak response of clenbuterol from *Sample solution 2*
C_S = concentration of Clenbuterol Hydrochloride in *Sample solution 2* (mg/mL)
C_U = concentration of Clenbuterol Hydrochloride in *Sample solution 1* (mg/mL)

Acceptance criteria
Individual impurities: 0.1%
Total impurities: NMT 0.2%
[NOTE—The reporting level for impurities is 0.05%.]

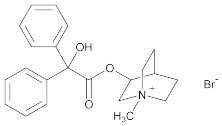
SPECIFIC TESTS

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
  Sample: 30 mg/mL in water, filter as necessary
  Acceptance criteria: −10° to +10° at 20°
- **pH** ⟨**791**⟩**:** 5.0–7.0
  Sample: 50 mg/mL in carbon dioxide-free water
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 1.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, protected from light. Store at room temperature.
- **LABELING:** Label it to indicate that it is for veterinary use only.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Clenbuterol Hydrochloride RS
  USP Clenbuterol Related Compound B RS
  1-(4-Amino-3,5-dichlorophenyl)-2-*tert*-butyl-aminoethanone hydrochloride.
  $C_{12}H_{16}Cl_2N_2O \cdot HCl$ 311.64

Clidinium Bromide



$C_{22}H_{26}BrNO_3$ 432.35
1-Azoniabicyclo[2.2.2]octane, 3-[(hydroxydiphenylacetyl)oxy]-1-methyl-, bromide, (±)-;
(±)-3-Hydroxy-1-methylquinuclidinium bromide benzilate [3485-62-9].

DEFINITION

Clidinium Bromide contains NLT 99.0% and NMT 100.5% of $C_{22}H_{26}BrNO_3$, calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B.** The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.
- **C. BROMIDE**
  Sample solution: 50 mg/mL
  Analysis: To 2 mL of the *Sample solution* add a few drops of 2 N nitric acid and 1 mL of silver nitrate TS.
  Acceptance criteria: A yellowish white precipitate is formed.

ASSAY

- **PROCEDURE**
  Sample: 1.2 g
  Analysis: Dissolve the *Sample* in 80 mL of glacial acetic acid, warming if necessary to effect solution. Cool, and add 15 mL of mercuric acetate TS. Titrate with 0.1 N perchloric acid in dioxane VS, determining the endpoint potentiometrically. Perform a blank determination (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 43.24 mg of $C_{22}H_{26}BrNO_3$.
  Acceptance criteria: 99.0%–100.5% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
- **HEAVY METALS** ⟨**231**⟩
  Sample solution: 1 g in 25 mL of water
  Acceptance criteria: NMT 20 ppm
- **ORGANIC IMPURITIES**
  Standard solution: 100 mg/mL of USP Clidinium Bromide RS in 0.1 N methanolic hydrochloric acid
  Sample solution: 100 mg/mL of Clidinium Bromide in 0.1 N methanolic hydrochloric acid
  Reference solution: Dissolve 100 mg of USP Clidinium Bromide RS in 1.0 mL of 0.1 N methanolic hydrochloric acid, and add 20 µL of a solution of 25.0 mg of USP Clidinium Bromide Related Compound A RS in 1.0 mL of 0.1 N methanolic hydrochloric acid.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)
  Adsorbent: 0.25-mm layer of chromatographic silica gel mixture
  Application volume: 20 µL
  Developing solvent system: Acetone, methanol, hydrochloric acid, and water (70:20:5:5)
  Spray reagent: Dissolve 850 mg of bismuth subnitrate in a mixture of 10 mL of glacial acetic acid and 40 mL of water. In a separate container, dissolve 20 g of potassium iodide in 50 mL of water. Mix the two solutions, and dilute with dilute sulfuric acid (1 in 10) to 500 mL. Add 7.5 g ± 2.5 g of iodine, and mix until the solution is complete.
  Chromatographic plates: Predevelop suitable thin-layer chromatographic plates by placing in a chromatographic chamber saturated with the *Developing solvent system*, and allow the *Developing solvent system* to move about 15 cm. Remove the plates from the chamber, dry at 105° for 15 min, and cool.
  Analysis 1 (3-quinuclidinyl benzilate): Apply the *Standard solution* and the *Sample solution* to a *Chromatographic plate*. Place the plate in an unsaturated chromatographic chamber containing freshly prepared *Developing solvent system*, and allow the solvent front to move 10 cm. Remove the plate, dry at 105° for 10 min, cool, and spray with potassium iodoplatinate TS.
  Acceptance criteria 1: The *Sample solution* shows no spot at an R_F value (about 0.8) corresponding to that of 3-quinuclidinyl benzilate.
  Analysis 2 (limit of clidinium bromide related compound A): Apply the *Sample solution* and *Reference solution* to a second *Chromatographic plate*. Place the plate in an unsaturated chromatographic chamber containing freshly prepared *Developing solvent system*, and allow the solvent front to move 15 cm. Remove the plate, dry at 105° for 10 min, cool, and spray with the *Spray reagent.*