IMPURITIES

• **Organic Impurities**

Standard solution A: 0.580 mg/mL of USP Albuterol Sulfate RS in water, equivalent to 0.483 mg/mL of albuterol

Standard solution B: 0.218 mg/mL of USP Albuterol Sulfate RS in water, equivalent to 0.183 mg/mL of albuterol

Standard solution C: 0.073 mg/mL of USP Albuterol Sulfate RS in water, equivalent to 0.061 mg/mL of albuterol

Sample solution: Place a quantity of finely powdered Tablets, equivalent to 48 mg of albuterol, into a suitable container. Add 60 mL of diluted alcohol (1 in 2), and shake by mechanical means for 30 min. Filter the mixture, and wash the filter with small portions of alcohol, combining this with the filtrate. Evaporate the filtrate to dryness under reduced pressure below 40°. Dissolve the residue as completely as possible in 2 mL of water.

Chromatographic system

(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 10 µL. Apply two successive 5-µL aliquots, allowing the solvent to evaporate between applications.

Developing solvent system: Methyl isobutyl ketone, isopropyl alcohol, ethyl acetate, ammonium hydroxide, and water (50:45:35:3:18)

Spray reagent A: 3-Methyl-2-benzothiazolinone hydrazone hydrochloride TS

Spray reagent B: Ammoniacal potassium ferricyanide TS

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*

Air-dry the plate. Develop the chromatograms until the solvent front has moved about 17 cm. Spray the plate first with *Spray reagent A*, and then *Spray reagent B*, and finally again with *Spray reagent A*. Examine the plate and estimate the responses of any secondary spots observed in the lane of the *Sample solution* by comparison with those of *Standard solutions A*, *B*, and *C*.

Acceptance criteria

1. 2.0%; no major secondary spot is greater in size or intensity than the principal spot produced by *Standard solution A*.
2. 0.75%; no other secondary spot is greater in size or intensity than the principal spot produced by *Standard solution B*.
3. 0.25%; no more than two other secondary spots are equal in size or intensity to the principal spot produced by *Standard solution C*.
4. The sum of the intensities of all secondary spots obtained from the *Sample solution* corresponds to NMT 3.5%.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Albuterol Sulfate RS

Albuterol Extended-Release Tablets

DEFINITION

Albuterol Extended-Release Tablets contain albuterol sulfate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of albuterol ($C_{13}H_{21}NO_3$).

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. Ultraviolet Absorption** ⟨197U⟩

Standard solution: 80 µg/mL of albuterol from USP Albuterol Sulfate RS in methanol

Sample solution: 80 µg/mL of albuterol in methanol, prepared as follows. Transfer a suitable number of Tablets to a volumetric flask, and dilute with methanol to volume. Stir for 30 min, and centrifuge.

Wavelength range: 210–350 nm

Cell path: 0.2 cm

Acceptance criteria: The *Sample solution* exhibits maxima and minima only at the same wavelengths as the *Standard solution*.

ASSAY

• **Procedure**

Buffer: 0.65 g/L of sodium 1-octane sulfonate and 21.7 g/L of ammonium acetate in water

Mobile phase: Glacial acetic acid, 2-propanol, methanol, and *Buffer* (4:3:1:92)

Diluent: 10 mL/L of triethylamine in water

Standard stock solution: 0.2 mg/mL of USP Albuterol Sulfate RS in *Diluent*

Standard solution: 0.02 mg/mL of USP Albuterol Sulfate RS in *Diluent*, from the *Standard stock solution*. Transfer an aliquot of the *Standard stock solution* to a suitable volumetric flask, and add 4% of the flask volume of methanol. Allow to cool to room temperature, and dilute with *Diluent* to volume.

Sample solution: Nominally 0.016 mg/mL of albuterol, prepared as follows. Transfer Tablets (NLT 10) to a suitable volumetric flask, add 10% of the flask volume of methanol, and sonicate for 30 min with regular swirling. Add 60% of the flask volume of *Diluent*, and sonicate for 30 min with swirling. Stir for 60 min, allow the solution to cool to room temperature, and dilute with *Diluent* to volume. Centrifuge a portion of this solution at 2500 rpm for 15 min. Transfer 10 mL of the supernatant into a 50-mL volumetric flask, add 1 mL of methanol, cool to room temperature, and dilute with *Diluent* to volume. Pass the solution though a 1-µm glass fiber or equivalent filter, and discard the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 276 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 40 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

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 albuterol ($C_{13}H_{21}NO_3$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Albuterol Sulfate RS in the *Standard solution* (mg/mL)

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

M = moles of albuterol per mole of albuterol sulfate, 2