Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-5B5ADF89-91C2-47E5-8526-C701A07928DE_4_en-US
DOI: https://doi.org/10.31003/USPNF_M31180_04_01
DOI Ref: vh8hb

Ethambutol Hydrochloride Tablets

DEFINITION
Ethambutol Hydrochloride Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2 \cdot 2HCl$).

IDENTIFICATION
Sample: Triturate a quantity equivalent to 100 mg of ethambutol from powdered Tablets, with 3 mL of methanol in a glass mortar. Add 5 mL of methanol to obtain a suspension, then pass through a funnel lined with a suitable filter paper (Whatman No. 42 or equivalent) previously moistened with methanol, and collect the filtrate in a beaker containing 100 mL of acetone. Stir the mixture, and allow crystallization to proceed for 15 min. Decant the liquid, and gently dry the crystals with the aid of a current of air until the odor of methanol is no longer detectable: a portion of the crystals so obtained responds to the following tests.

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** **Identification Tests—General, *Chloride*⟨191⟩**
Sample solution: 100 mg/mL in water
Acceptance criteria: Meet the requirement

ASSAY
• **Procedure**
Buffer: Mix 1.0 mL of triethylamine with 1 L of water, and adjust with phosphoric acid to pH 7.0.
Mobile phase: Acetonitrile and *Buffer* (1:1)
Standard solution: 0.30 mg/mL of USP Ethambutol Hydrochloride RS
Sample solution: Equivalent to 0.30 mg/mL of ethambutol hydrochloride from powdered Tablets (NLT 20). Filter the solution, discarding the first 10-mL portion.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 200 nm
Column: 4.6-mm × 15-cm base-deactivated; 5-µm packing L10
Flow rate: 1 mL/min
Injection volume: 50 µL
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 ethambutol hydrochloride ($C_{10}H_{24}N_2O_2 \cdot 2HCl$) present in the portion of Tablets 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 Ethambutol Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ethambutol hydrochloride from the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer: 38.0 g/L of monobasic sodium phosphate and 2.0 g/L of anhydrous dibasic sodium phosphate

Bromocresol green solution: Dissolve 200 mg of bromocresol green in 30 mL of water and 6.5 mL of 0.1 N sodium hydroxide. Dilute with *Buffer* to 500 mL, and add 0.1 N hydrochloric acid to adjust to a pH of 4.6 ± 0.1.

Standard solution: 0.1 mg/mL of USP Ethambutol Hydrochloride RS

Sample solution: Pass a portion of solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: Vis

Analytical wavelength: 415 nm

Analysis

Samples: *Standard solution*, *Sample solution*, and water (blank)

Into 3 separate, glass-stoppered, 50-mL centrifuge tubes, pipet 1 mL of water to provide the blank, 1 mL of *Standard solution*, and 1 mL of *Sample solution*. Add 5.0 mL of *Bromocresol green solution* to each tube, add 10.0 mL of chloroform to each, insert the stoppers, and shake the mixtures vigorously. Allow the mixtures to separate, discard the upper aqueous layers, and filter the 3 chloroform layers through separate pledgets of cotton.

Determine the the percentage of the labeled amount of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2 \cdot 2HCl$) dissolved, using the blank to set the instrument.

Tolerances: NLT 75% (*Q*) of the labeled amount of $C_{10}H_{24}N_2O_2 \cdot 2HCl$ is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Limit of Aminobutanol**

Buffer: 1.24 g of boric acid to a 100-mL volumetric flask. Dissolve in 90 mL of water, adjust with 5 N sodium hydroxide to a pH of 9.0, and dilute with water to volume.

Fluorescamine solution: 0.1 mg/mL of fluorescamine in acetone

Standard solution: 5.0 µg/mL of USP Aminobutanol RS in water

Sample solution: Place a number of Tablets, equivalent to 400 mg of ethambutol hydrochloride, in a beaker, cover with acetone, and allow to stand for 15 min. Decant the acetone, dry the Tablets, and remove the coating. Grind the Tablet cores in a mortar to a fine powder, moisten with methanol, and triturate to a fine paste. Transfer the mixture with the aid of methanol to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Pass the mixture through a dry, folded filter paper. Pipet 25 mL of the filtrate into a 200-mL volumetric flask, and dilute with water to volume. Allow to stand for 15 min, and pass through a dry, folded filter paper, discarding the first cloudy portions of the filtrate. The clear filtrate is the *Sample solution*.

Instrumental conditions

(See *Fluorescence Spectroscopy* ⟨853⟩.)

Mode: Fluorometry

Analytical wavelength: Excitation wavelength at about 385 nm; emission wavelength at 485 nm

Cell: 1 cm

Analysis

Samples: *Standard solution* and *Sample solution*

Pipet a 10-mL portion of the *Sample solution* into a glass-stoppered, 100-mL conical flask, and add 10 mL of water and 20 mL of *Buffer*. To another 100-mL flask, add 10.0 mL of the *Sample solution*, 10.0 mL of the *Standard solution*, and 20 mL of *Buffer*. Place the flasks on a magnetic stirrer, and while the contents are being stirred rapidly, add 10 mL of *Fluorescamine solution* rapidly. Insert the stoppers in the flasks, invert, and shake briefly. After 1 min, accurately timed, determine the relative fluorescence intensities of both solutions.

Acceptance criteria: The fluorescence intensity of the solution from the *Sample solution* is NMT the difference between the intensities of the two solutions; NMT 1.0%.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Aminobutanol RS

USP Ethambutol Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ETHAMBUTOL HYDROCHLORIDE TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 28(5)

Current DocID: GUID-5B5ADF89-91C2-47E5-8526-C701A07928DE_4_en-US

DOI: https://doi.org/10.31003/USPNF_M31180_04_01

DOI ref: vh8hb