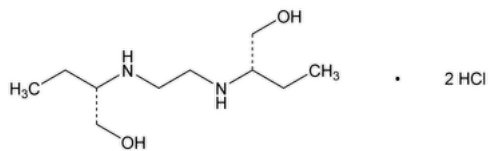


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Ethambutol Hydrochloride



$C_{10}H_{24}N_2O_2 \cdot 2HCl$ 277.23
1-Butanol, 2,2'-(1,2-ethanediylidimino)bis-, dihydrochloride, [S-(R*,R*)]-;
(+)-2,2'-(Ethylenediimino)-di-1-butanol dihydrochloride;
(2S,2'S)-2,2'-[Ethane-1,2-diylbis(azanediyl)]dibutan-1-ol CAS RN®: 1070-11-7; UNII: QE4VW5F007.

DEFINITION

Ethambutol Hydrochloride contains NLT 98.0% and NMT 100.5% of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2 \cdot 2HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K
- **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

Sample solution: 100 mg/mL in water

Acceptance criteria: Meets the requirements

ASSAY

• **PROCEDURE**

Sample solution: 200 mg of Ethambutol Hydrochloride in a mixture of 100 mL of [glacial acetic acid](#) and 5 mL of [mercuric acetate TS](#). Add [crystal violet TS](#).

Analysis: Titrate with 0.1 N [perchloric acid VS](#) (the color change at the endpoint is from blue to blue-green). Perform a blank determination, and make any necessary corrections (see [Titrimetry \(541\)](#)). Each milliliter of 0.1 N perchloric acid is equivalent to 13.86 mg of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2 \cdot 2HCl$).

Acceptance criteria: 98.0%–100.5% on the dried basis

IMPURITIES

• **ORGANIC IMPURITIES**

Protect all solutions containing ethambutol from light.

Solution A: [Methanol](#) and [water](#) (50:50)

Solution B: [Methanol](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	82	18
30	82	18
35	0	100
37	0	100
38	82	18
50	82	18

Impurity stock solution A: To 4 mg of [USP Ethambutol Related Compound A RS](#), add 4 mL of [acetonitrile](#) and 0.1 mL of [triethylamine](#).

Sonicate for 5 min and add 15 µL of [\(R\)-\(+\)-alpha-methylbenzyl isocyanate](#). Heat the mixture at 70° for 20 min.

Impurity stock solution B: To 4 mg of [USP Ethambutol Related Compound B RS](#), add 4 mL of [acetonitrile](#) and 0.1 mL of [triethylamine](#).

Sonicate for 5 min and add 15 µL of [\(R\)-\(+\)-alpha-methylbenzyl isocyanate](#). Heat the mixture at 70° for 20 min.

System suitability solution: To 4 mg of [USP Ethambutol Hydrochloride RS](#), add 4 mL of [acetonitrile](#) and 0.1 mL of [triethylamine](#). Sonicate for 5 min and add 15 µL of [\(R\)-\(+\)-alpha-methylbenzyl isocyanate](#). Heat the mixture at 70° for 20 min. Add 40 µL each of *Impurity stock solution A* and *Impurity stock solution B*.

Standard stock solution: To 4 mg of [USP Ethambutol Hydrochloride RS](#), add 4 mL of [acetonitrile](#) and 0.1 mL of [triethylamine](#). Sonicate for 5 min and add 15 µL of [\(R\)-\(+\)-alpha-methylbenzyl isocyanate](#). Heat the mixture at 70° for 20 min.

Standard solution: Dilute 0.5 mL of *Standard stock solution* with [acetonitrile](#) to 100.0 mL.

Sample solution: To 4 mg of Ethambutol Hydrochloride, add 4 mL of [acetonitrile](#) and 0.1 mL of [triethylamine](#). Sonicate for 5 min and add 15 µL of [\(R\)-\(+\)-alpha-methylbenzyl isocyanate](#). Heat the mixture at 70° for 20 min.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 10-cm; 3-µm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for ethambutol related compound B, ethambutol, and ethambutol related compound A are 0.91, 1.0, and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.2 between ethambutol related compound B and ethambutol; NLT 3.0 between ethambutol and ethambutol related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Ethambutol Hydrochloride taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

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

C_S = concentration of [USP Ethambutol Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: See [Table 2](#). The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ethambutol	1.0	—
Ethambutol related compound A	1.3	1.0
Any individual impurity ^a	—	0.10
Total impurities ^a	—	1.0

^a Calculate any individual impurity and total impurities from the relative retention times of 0.75 to 1.5 with reference to ethambutol.

Change to read:

• LIMIT OF AMINOBUTANOL