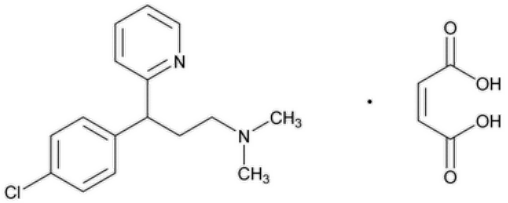
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-6550B924-ED46-4BA0-8B4B-9B9AE744C712_6_en-US
DOI: https://doi.org/10.31003/USPNF_M16450_06_01
DOI Ref: iyg6s

Chlorpheniramine Maleate



$C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ 390.86

2-Pyridinepropanamine, γ-(4-chlorophenyl)-*N*,*N*-dimethyl-, (*Z*)-2-butenedioate (1:1);

2-[*p*-Chloro-α-[2-(dimethylamino)ethyl]benzyl] pyridine maleate (1:1) CAS RN®: 113-92-8; UNII: V1Q0O9OJ9Z.

DEFINITION

Chlorpheniramine Maleate contains NLT 98.0% and NMT 102.0% of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention times of the maleic acid and chlorpheniramine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 5.44 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile

Diluent: Acetonitrile and *Solution A* (5:95)

System suitability stock solution: 0.02 mg/mL each of USP Pheniramine Maleate RS, USP Chlorpheniramine Related Compound B RS, and USP Chlorpheniramine Related Compound C RS in *Diluent*. Sonicate for 1 min.

System suitability solution: 0.5 mg/mL of USP Chlorpheniramine Maleate RS and 2 µg/mL each of USP Pheniramine Maleate RS, USP Chlorpheniramine Related Compound B RS, and USP Chlorpheniramine Related Compound C RS in *Diluent*, prepared as follows. Transfer 5.0 mg of USP Chlorpheniramine Maleate RS to a 10-mL volumetric flask, add 5 mL of *Diluent* and 1.0 mL of the *System suitability stock solution*, and dilute with *Diluent* to volume. Sonicate for 1 min.

Standard solution: 0.5 mg/mL of USP Chlorpheniramine Maleate RS in *Diluent*. Sonicate for 1 min.

Sample solution: 0.5 mg/mL of Chlorpheniramine Maleate in *Diluent*. Sonicate for 1 min.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
1	95	5
20	70	30

Time (min)	Solution A (%)	Solution B (%)
30	70	30
31	95	5
40	95	5

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

[NOTE—The relative retention times of maleic acid, chlorpheniramine related compound C, and chlorpheniramine are 0.18, 0.94 and 1.0, respectively.]

Resolution: NLT 1.5 between chlorpheniramine related compound C and chlorpheniramine; and NLT 2.0 between chlorpheniramine related compound B and pheniramine, *System suitability solution*

Tailing factor: NMT 2.0 for chlorpheniramine, *Standard solution*

Relative standard deviation: NMT 0.73% for chlorpheniramine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) in the portion of Chlorpheniramine Maleate taken:

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

r_U = peak response of chlorpheniramine from the *Sample solution*

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

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

C_U = concentration of Chlorpheniramine Maleate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%
- **ORGANIC IMPURITIES**

Solution A, Solution B, Diluent, System suitability solution, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1.4 µg/mL of USP Chlorpheniramine Maleate RS in *Diluent*, equivalent to 1.0 µg/mL of chlorpheniramine. Sonicate for 1 min.

Sensitivity solution: 0.28 µg/mL of USP Chlorpheniramine Maleate RS in *Diluent*

Sample solution: 0.5 mg/mL of Chlorpheniramine Maleate in *Diluent*. Sonicate for 1 min.

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between chlorpheniramine related compound C and chlorpheniramine; and NLT 2.0 between the chlorpheniramine related compound B and pheniramine, *System suitability solution*

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

Signal-to-noise ratio: NLT 10 for chlorpheniramine, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Chlorpheniramine Maleate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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

C_S = concentration of chlorpheniramine from the *Standard solution* (mg/mL)

C_U = concentration of Chlorpheniramine Maleate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks having areas less than 0.05% that of chlorpheniramine.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Maleic acid[a]	0.18	—	—
Diamine analog[b]	0.37	0.73	0.2
Chlorpheniramine related compound B[c]	0.49	0.77	0.1
Pheniramine[d]	0.57	—	—
Chlorpheniramine related compound C[e]	0.97	1.0	0.1
Chlorpheniramine	1.0	—	—
Chlorpheniramine nitrile[f]	1.19	1.0	0.1
Any other unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] Salt counter ion is included in the table for identification purposes only.

[b] 2-(4-Chlorophenyl)-4-(dimethylamino)-2-[2-(dimethylamino)ethyl]butanenitrile.

[c] Di(pyridin-2-yl)amine.

[d] Used only to establish the system suitability.

[e] 3-(4-Chlorophenyl)-*N*-methyl-3-(pyridin-2-yl)propan-1-amine.

[f] 2-(4-Chlorophenyl)-4-(dimethylamino)-2-(pyridin-2-yl)butanenitrile.

SPECIFIC TESTS

- **Optical Rotation ⟨781⟩**

  Sample: 100 mg/mL in water at 20°

  Acceptance criteria: −0.10° to +0.10°

- **Loss on Drying ⟨731⟩**

  Analysis: Dry at 105° for 3 h.

  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Chlorpheniramine Maleate RS

USP Chlorpheniramine Related Compound B RS

Di(pyridin-2-yl)amine.

$C_{10}H_9N_3$ 171.20

USP Chlorpheniramine Related Compound C RS

▲3-(4-Chlorophenyl)-*N*-methyl-3-(pyridin-2-yl)propan-1-amine maleate.

$C_{15}H_{17}ClN_2 \cdot C_4H_4O_4$ 376.83▲ (ERR 1-Dec-2017)

USP Pheniramine Maleate RS

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

Topic/Question	Contact	Expert Committee
CHLORPHENIRAMINE MALEATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(6)

Current DocID: GUID-6550B924-ED46-4BA0-8B4B-9B9AE744C712_6_en-US

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