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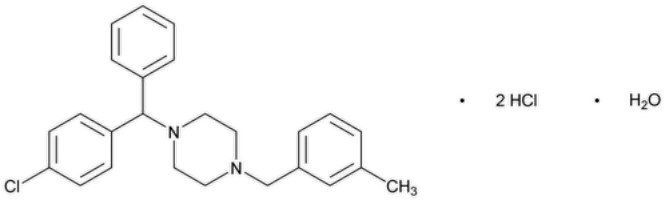
Meclizine Hydrochloride



• 2 HCl • H_2O

$C_{25}H_{27}ClN_2 \cdot 2HCl \cdot H_2O$ 481.89
$C_{25}H_{27}ClN_2 \cdot 2HCl$ 463.88

Piperazine, 1-[(4-chlorophenyl)phenylmethyl]-4-[(3-methylphenyl)methyl]-, dihydrochloride, monohydrate;
1-(*p*-Chloro-α-phenylbenzyl)-4-(*m*-methylbenzyl)piperazine dihydrochloride monohydrate CAS RN®: 31884-77-2; UNII: HDP7W44CIO.
Anhydrous CAS RN®: 1104-22-9; UNII: L997QXC9J1.

DEFINITION

Meclizine Hydrochloride contains NLT 97.0% and NMT 102.0% of $C_{25}H_{27}ClN_2 \cdot 2HCl$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** Identification Tests—General, *Chloride* ⟨191⟩

Sample solution: Dissolve 25 mg in a mixture of 3 mL of 2 N nitric acid and 5 mL of alcohol.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Dissolve 1.5 g of sodium 1-heptanesulfonate in 300 mL of water, and mix this solution with 700 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.

Standard solution: 0.1 mg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Meclizine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Flow rate: 1.3 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of meclizine hydrochloride ($C_{25}H_{27}ClN_2 \cdot 2HCl$) in the portion of Meclizine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities, Procedure 1**

[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended when the isomeclizine impurity may be present.]

Mobile phase: Dissolve 1.5 g of sodium 1-heptanesulfonate in 300 mL of water, and mix this solution with 700 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.

System suitability solution: 0.01 mg/mL each of USP Meclizine Hydrochloride RS and 4-chlorobenzophenone in *Mobile phase*

Standard solution: 2.5 µg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Meclizine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Flow rate: 1.3 mL/min

Injection size: 20 µL

System suitability

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

[Note—The elution order is meclizine, followed by 4-chlorobenzophenone.]

Suitability requirements

Resolution: NLT 2.0 between meclizine hydrochloride and 4-chlorobenzophenone, *System suitability solution*

Column efficiency: NLT 1800 theoretical plates, determined from the analyte peak, *Standard solution*

Tailing factor: NMT 1.5 for the analyte peak, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the *Sample solution* to elute for NLT three times the retention time of meclizine hydrochloride.

Calculate the percentage of each impurity in the portion of Meclizine Hydrochloride 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 meclizine from the *Standard solution*

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

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

F = relative response factor, 0.72 for the 4-chlorobenzophenone peak and 1.0 for all other peaks

Acceptance criteria

Any individual impurity: NMT 0.5%

Total impurities: NMT 1.0%

• **Organic Impurities, Procedure 2**

Mobile phase: Dissolve 5 g of sodium 1-heptanesulfonate in 1000 mL of water, and mix 600 mL of this solution with 400 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.0 ± 0.1.

System suitability solution: 2.5 µg/mL each of USP Meclizine Hydrochloride RS, USP Meclizine Related Compound A RS, and USP Meclizine Related Compound B RS in *Mobile phase*

Standard solution: 2.5 µg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Meclizine Hydrochloride in *Mobile phase*. [Note—Store this solution no longer than 24 h.]

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 50°

Flow rate: 2.0 mL/min

Injection size: 30 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between meclizine related compound B and meclizine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 6.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Meclizine Hydrochloride 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 meclizine from the *Standard solution*

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any peak eluting before 1.75 min.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
3-Methylbenzyl alcohol	0.11	1.0	0.10
1,4-Bis(3-methylbenzyl) piperazine	0.22	0.73	0.10
4-Chlorobenzhydrol[a]	0.53	1.3	0.15
Meclizine *o*-chloro isomer[b]	0.81	1.0	0.10
Isomeclizine (meclizine *o*-methyl isomer)[c]	0.90	1.1	0.15
Meclizine	1.0	—	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] USP Meclizine Related Compound A.

[b] 1-[2-Chlorophenyl)(phenyl)methyl]-4-(3-methylbenzyl) piperazine.

[c] USP Meclizine Related Compound B.

SPECIFIC TESTS

• **Water Determination, *Method I*⟨921⟩:** NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at room temperature.

• **Labeling:** If a test for *Organic Impurities* other than *Procedure 1* is used, the labeling states the test with which the article complies.

• **USP Reference Standards ⟨11⟩**

USP Meclizine Hydrochloride RS

USP Meclizine Related Compound A RS

4-Chlorobenzhydrol.

$C_{13}H_{11}ClO$ 218.68

USP Meclizine Related Compound B RS

Isomeclizine

1-[(4-Chlorophenyl)(phenyl)methyl]-4-(2-methylbenzyl)piperazine dihydrochloride monohydrate.

$C_{25}H_{27}ClN_2 \cdot 2HCl \cdot H_2O$ 481.88

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

Topic/Question	Contact	Expert Committee
MECLIZINE HYDROCHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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