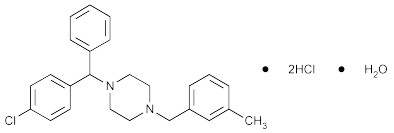
Meclizine Hydrochloride



$C_{25}H_{27}ClN_2 \cdot 2HCl \cdot H_2O$ 481.88
Piperazine, 1-[(4-chlorophenyl)phenylmethyl]-4-[(3-methylphenyl)methyl]-, dihydrochloride, monohydrate.
1-(*p*-Chloro-α-phenylbenzyl)-4-(*m*-methylbenzyl)piperazine dihydrochloride monohydrate [31884-77-2].
Anhydrous 463.88 [1104-22-9].

» Meclizine Hydrochloride contains not less than 97.0 percent and not more than 100.5 percent of $C_{25}H_{27}ClN_2 \cdot 2HCl$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**
USP Meclizine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg per mL.

Medium: dilute hydrochloric acid (1 in 100).

C: Dissolve 25 mg in a mixture of 3 mL of 2 N nitric acid and 5 mL of alcohol: the solution meets the requirements of the tests for *Chloride* ⟨191⟩.

Water, *Method I* ⟨921⟩: not more than 5.0%.

Residue on ignition ⟨281⟩: not more than 0.1%.

Chromatographic purity—

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, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve an accurately weighed quantity of USP Meclizine Hydrochloride RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 2.5 µg per mL.

Test solution—Prepare a solution of Meclizine Hydrochloride in *Mobile phase* having a known concentration of about 0.5 mg per mL.

System suitability solution—Prepare a solution in *Mobile phase* containing about 0.01 mg of USP Meclizine Hydrochloride RS and 0.01 mg of 4-chlorobenzophenone per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.3 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the elution order is meclizine, followed by 4-chlorobenzophenone; and the resolution, *R,* between the 4-chlorobenzophenone and meclizine hydrochloride peaks is not less than 2.0. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the tailing factor for the analyte peak is not more than 1.5; the column efficiency, *N,* determined from the analyte peak is not less than 1800 theoretical plates; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph. Allow the *Test solution* to elute for not less than three times the retention time of meclizine hydrochloride. Record the chromatograms and measure all of the peak areas. Calculate the percentage of each impurity in the portion of Meclizine Hydrochloride taken by the formula:

$$100(1/F)(0.001C_S / C_U)(r_U / r_S)$$

in which F is the relative response factor, which is equal to 0.72 for the 4-chlorobenzophenone peak and 1.0 for all other peaks; C_S is the concentration, in µg per mL, of meclizine hydrochloride in the *Standard solution,* and the multiplier of 0.001 is for conversion of µg per mL to mg per mL; C_U is the concentration, in mg per mL, of Meclizine Hydrochloride in the *Test solution;* r_U is the peak response for each impurity obtained from the *Test solution;* and r_S is the response of the meclizine peak obtained from the *Standard solution:* not more than 0.5% of any single impurity is found, and not more than 1.0% of total impurities is found.

Assay—Dissolve about 350 mg of Meclizine Hydrochloride, accurately weighed, in about 50 mL of chloroform. Add 50 mL of glacial acetic acid, 5 mL of acetic anhydride, and 10 mL of mercuric acetate TS, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically, using a calomel-glass electrode system (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 23.19 mg of $C_{25}H_{27}ClN_2 \cdot 2HCl$.

Meclizine Hydrochloride Tablets

» Meclizine Hydrochloride Tablets contain not less than 95.0 percent and not more than 110.0 percent of the labeled amount of meclizine hydrochloride ($C_{25}H_{27}ClN_2 \cdot 2HCl$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Meclizine Hydrochloride RS

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

B: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Adsorbent: 0.5-mm layer of chromatographic silica gel mixture.

Test solution—Extract a quantity of finely powdered Tablets, equivalent to about 125 mg of meclizine hydrochloride, by shaking for 15 minutes with 50 mL of methanol.

Standard solution—Prepare a solution of USP Meclizine Hydrochloride RS in methanol, containing 2.5 mg per mL.

Application volume: 50 µL.

Developing solvent system: a mixture of cyclohexane, toluene, and diethylamine (15:3:2).

Procedure—Proceed as directed in the chapter, except to place the plate in a developing chamber that contains and has been equilibrated with *Developing solvent system.*

Dissolution, *Procedure for a Pooled Sample* ⟨711⟩**—**

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Determine the amount of $C_{25}H_{27}ClN_2 \cdot 2HCl$ dissolved by employing the following method.

Mobile phase—Prepare a suitable degassed and filtered mixture of water and methanol (55:45) that contains 0.69 g of monobasic sodium phosphate in each 100 mL and is adjusted with phosphoric acid, if necessary, to a pH of 4.0.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector and