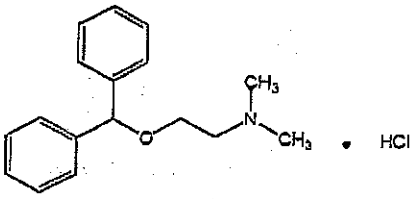
Diphenhydramine Hydrochloride



$C_{17}H_{21}NO \cdot HCl$ 291.82
Ethanamine, 2-(diphenylmethoxy)-*N,N*-dimethyl-, hydrochloride.
2-(Diphenylmethoxy)-*N,N*-dimethylethylamine hydrochloride [*147-24-0*].

>> Diphenhydramine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{17}H_{21}NO \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at room temperature.
USP Reference standards <11>—*USP Diphenhydramine Hydrochloride RS.*
Identification—
A: It meets the requirements under *Identification—Organic Nitrogenous Bases* <181>
B: 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*.
C: It responds to the tests for *Chloride* <191>.
Melting range <741>: between 167° and 172°.
Loss on drying <731>—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.
Residue on ignition <281>: not more than 0.1%.
Organic volatile impurities, *Method I* <467>: meets the requirements.
(Official until July 1, 2008)
Assay—
Mobile phase—Prepare a solution of acetonitrile, water, and triethylamine (50:50:0.5), adjust with glacial acetic acid to a pH of 6.5, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).
Standard preparation — Dissolve an accurately weighed quantity of USP Diphenhydramine Hydrochloride RS in water to obtain a solution having a known concentration of about 0.5 mg per mL.
Assay preparation — Transfer about 25 mg of Diphenhydramine Hydrochloride, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with water to volume, mix, and filter.
System suitability solution—Dissolve about 5 mg of benzophenone in 5 mL of acetonitrile, dilute with water to 100 mL, and mix. Transfer 1.0 mL of this solution and 5 mg of diphenhydramine hydrochloride to a 10-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L10. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R*, between the benzophenone and diphenhydramine peaks is not less than 2.0. Chromatograph replicate injections of the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2.0%; and the tailing factor for the diphenhydramine hydrochloride peak is not more than 2.0.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{17}H_{21}NO \cdot HCl$ in the portion of Diphenhydramine Hydrochloride taken by the formula:

$$50C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Diphenhydramine Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.