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Dimenhydrinate Injection

» Dimenhydrinate Injection is a solution of Dimenhydrinate in a mixture of Propylene Glycol and water. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I or Type III glass.

USP Reference standards ⟨11⟩—

USP Dimenhydrinate RS

Identification—The relative retention times of the major peaks for 8-chlorotheophylline and diphenhydramine in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

pH ⟨791⟩**:** between 6.4 and 7.2.

Content of 8-chlorotheophylline—

Mobile phase—Dissolve 0.81 g of *dl*-10-camphorsulfonic acid and 0.70 g of sodium acetate in 700 mL of water. Add 300 mL of methanol, mix, and pass through a membrane filter having a 0.5-µm or finer porosity.

Standard solution—Dissolve an accurately weighed quantity of USP Dimenhydrinate RS in methanol to obtain a Standard stock solution having a known concentration of about 0.5 mg per mL. Retain a portion of this Standard stock solution for use in the *Assay.* Pipet 5 mL into a 50-mL volumetric flask, dilute with methanol to volume, mix, and pass through a membrane filter having a 0.5-µm or finer porosity.

Test solution—Transfer an accurately measured volume of Injection, equivalent to about 50 mg of dimenhydrinate, to a 100-mL volumetric flask, dilute with methanol to volume, and mix to obtain a stock solution. Retain a portion of this stock solution for use in the *Assay.* Pipet 5 mL of this stock solution into a 50-mL volumetric flask, dilute with methanol to volume, mix, and pass through a membrane filter having a 0.5-µm or finer porosity.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector, a 2-mm × 12.5-cm guard column that contains packing L2, and a 4.6-mm × 25-cm analytical column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph three replicate injections of the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 1.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of 8-chlorotheophylline ($C_7H_7ClN_4O_2$) in each mL of the Injection taken by the formula:

$$(214.61/469.96)(1000C/V)(r_U/r_S)$$

in which 214.61 and 469.96 are the molecular weights of 8-chlorotheophylline and dimenhydrinate, respectively; C is the concentration, in mg per mL, of USP Dimenhydrinate RS in the *Standard solution; V* is the volume, in mL, of Injection taken; and r_U and r_S are the peak responses obtained from the *Test solution* and the *Standard solution*, respectively. An amount of 8-chlorotheophylline that is between 43.4% and 47.9% of the amount of dimenhydrinate obtained in the *Assay* is found.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

Change to read:

Assay—

▲*Solution A*—Dissolve 0.8 g of ammonium bicarbonate in 800 mL of water. Add 200 mL of methanol, filter, and degas.

Solution B—Dissolve 0.8 g of ammonium bicarbonate in 150 mL of water. Add 850 mL of methanol, filter, and degas.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution in methanol containing 2.0 mg of 2-hydroxybenzyl alcohol per mL.▲ (ERR 1-Sep-2021)

Standard preparation—Use a portion of the Standard stock solution that was prepared for the *Standard solution* in the test for *Content of 8-chlorotheophylline.* Mix 5.0 mL of this Standard stock solution and 5.0 mL of *Internal standard solution*, and pass through a membrane filter having a 0.5-µm or finer porosity.

Assay preparation—Use a portion of the stock solution that was prepared for the *Test solution* in the test for *Content of 8-chlorotheophylline.* Mix 5.0 mL of this stock solution and 5.0 mL of *Internal standard solution*, and pass through a membrane filter having a 0.5-µm or finer porosity.

▲*Chromatographic system* (see *Chromatography* ⟨621⟩)— The liquid chromatograph is equipped with a 229-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0	100	0	equilibration
0–7.0	100	0	isocratic
7.0–7.1	100→0	0→100	linear gradient
7.1–15	0	100	isocratic
15–15.1	0→100	100→0	linear gradient
15.1–22.0	100	0	isocratic

Chromatograph the *Standard preparation*, and record the peak areas as directed for *Procedure*: the relative retention times are about 0.3 for 8-chlorotheophylline, 0.5 for the internal standard, and 1.0 for diphenhydramine; the resolution, *R*, between 8-chlorotheophylline and the internal standard is not less than 4.5; and the relative standard deviation for replicate injections is not more than 2.0%.▲ (ERR 1-Sep-2021)

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 areas for the major peaks.▲ (ERR 1-Sep-2021) Calculate the quantity, in mg, of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$) in each mL of the Injection taken by the formula:

$$(200C/V)(R_U/R_S)$$

in which *C* is the concentration of USP Dimenhydrinate RS in the *Standard preparation*; *V* is the volume, in mL, of Injection taken; and ▲R_U and R_S are the peak area ratios of diphenhydramine to the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.▲ (ERR 1-Sep-2021)

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

Topic/Question	Contact	Expert Committee
DIMENHYDRINATE INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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