Dimenhydrinate Oral Solution

> Dimenhydrinate Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of dimenhydrinate (C₁₇H₂₁NO·C₇H₇ClN₄O₂).

**Packaging and storage**—Preserve in tight containers.

**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.

**Content of 8-chlorotheophylline**—

Ammonium bicarbonate solution, Diluent, Solution A, Solution B, Mobile phase, Internal standard solution, and Chromatographic system—Proceed as directed in the Assay under Dimenhydrinate Tablets.

Standard solution—Prepare as directed for Standard preparation in the Assay under Dimenhydrinate Tablets.

Test solution—Prepare as directed for Assay preparation in the Assay.

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 areas for the major peaks. Calculate the quantity, in mg per mL, of 8-chlorotheophylline (C₁₇H₂₁NO·C₇H₇ClN₄O₂) in the portion of Oral Solution taken by the formula:

\[
(214.61/469.96)(0.05W_{R_i}/R_i)
\]

in which 214.61 and 469.96 are the molecular weights of 8-chlorotheophylline and dimenhydrinate, respectively; \(W\) is the weight, in mg, of USP Dimenhydrinate RS in the Standard solution; and \(R_i\) and \(R_i\) are the peak area ratios of diphenhydramine to the internal standard obtained from the Assay preparation and the Standard preparation, respectively.

**Dimenhydrinate Tablets**

> Dimenhydrinate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of dimenhydrinate (C₁₇H₂₁NO·C₇H₇ClN₄O₂).

**Packaging and storage**—Preserve in well-closed containers.

**USP Reference standards** (11)—

USP Dimenhydrinate RS

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

**Dissolution** (711)—

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of C₁₇H₂₁NO·C₇H₇ClN₄O₂ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 276 nm on filtered portions of the solution under test, suitably diluted with Dissolution Medium, if necessary, in comparison with a Standard solution having a known concentration of USP Dimenhydrinate RS in the same Medium.

Tolerances—Not less than 75% (Q) of the labeled amount of C₁₇H₂₁NO·C₇H₇ClN₄O₂ is dissolved in 45 minutes.

**Uniformity of dosage units** (905): meet the requirements, the following procedure being used where the test for **Content Uniformity** is required. Transfer 1 Tablet to a 50-mL volumetric flask, add about 5 mL of Ammonium bicarbonate solution obtained from the Assay, and shake gently to disperse, sonicating, if necessary. Add 20.0 mL of Internal standard solution obtained from the Assay, shake by mechanical means for 30 minutes, and centrifuge. To 1 mL of the clear supernatant add about 9 mL of Diluent obtained from the Assay, and mix. Continue as directed for Procedure in the Assay.

**Content of 8-chlorotheophylline**—

Ammonium bicarbonate solution, Diluent, Solution A, Solution B, Mobile phase, Internal standard solution, and Chromatographic system—Prepare as directed in the **Assay**.


Test solution—Prepare as directed for Assay preparation in the Assay.

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 areas for the major peaks. Calculate the quantity, in mg, of 8-chlorotheophylline (C₁₇H₂₁NO·C₇H₇ClN₄O₂) per Tablet taken by the formula:

\[
(214.61/469.96)W_{R_i}/R_i
\]

in which 214.61 and 469.96 are the molecular weights of 8-chlorotheophylline and dimenhydrinate, respectively; \(W\) is the weight, in mg, of USP Dimenhydrinate RS in the Standard solution.
tion; and $R_0$ and $R_i$ are peak area ratios of 8-chlorotheophylline to the internal standard 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.

**Assay**

Ammonium bicarbonate solution—Dissolve 4 g of ammonium bicarbonate in 250 mL of water.

Diluent—Dissolve 4 g of ammonium bicarbonate in 200 mL of water. Add 50 mL of methanol, and mix.

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.

Standard preparation—Accurately weigh about 50 mg of USP Dimenhydrinate RS, add about 5 mL of Ammonium bicarbonate solution and 20.0 mL of Internal standard solution, and mix. To 1 mL of this solution add about 9 mL of Diluent, and mix.

Assay preparation—Transfer 5 Tablets into a 250-mL volumetric flask, add 25 mL of Ammonium bicarbonate solution, and shake gently to disperse, sonicating if necessary. Add 100.0 mL of Internal standard solution, shake vigorously for 30 minutes, and centrifuge. To 1 mL of the clear supernatant add about 9 mL of Diluent, and mix.

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 chromatogram is programmed as follows.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
<th>Elution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>0</td>
<td>equilibration</td>
</tr>
<tr>
<td>0–7.0</td>
<td>100</td>
<td>0</td>
<td>isocratic</td>
</tr>
<tr>
<td>7.0–7.1</td>
<td>0–100</td>
<td>0–100</td>
<td>linear gradient</td>
</tr>
<tr>
<td>7.1–15</td>
<td>0</td>
<td>100</td>
<td>isocratic</td>
</tr>
<tr>
<td>15–15.1</td>
<td>0</td>
<td>100</td>
<td>linear gradient</td>
</tr>
<tr>
<td>15.1–22.0</td>
<td>0</td>
<td>100</td>
<td>isocratic</td>
</tr>
</tbody>
</table>

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, $R_i$, 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%.

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. Calculate the quantity, in mg, of dimenhydrinate (C_{12}H_{22}NO_3-CH_{3}CIN-O) per Tablet taken by the formula:

$$W(R_0 / R_i)$$

in which $W$ is the weight, in mg, of USP Dimenhydrinate RS in the Standard preparation; and $R_0$ and $R_i$ are the peak area ratios of diphenhydramine to the internal standard obtained from the Assay preparation and the Standard preparation, respectively.

**Dimercaprol**

$$\text{C}_9\text{H}_{16}\text{O}_4\text{S}_2\text{S}_2\text{O}_4\text{S}_2$$

1-Propanol, 2,3-dimercapto.

2,3-Dimercapto-1-propanol [59-52-9].

» Dimercaprol contains not less than 97.0 percent and not more than 100.5 percent of C_{12}H_{16}O_4S_2, and not more than 1.5 percent of 1,2,3-trimercaptopropane (C_{13}H_{15}S_3).

**Packaging and Storage**— Preserve in tight containers, in a cold place.

**Specific gravity** (841): between 1.242 and 1.244.

**Distilling range**, Method I (721): between 66 ° and 68 °, under a pressure of 0.2 mm of mercury.

**Refractive index** (831): between 1.567 and 1.573.

**Limit of 1,2,3-trimercaptopropane and related impurities**

Adsorbent—Use a suitable chromatographic grade of 100-mesh silicic acid.

Standard buffer solution—Prepare 100 mL of pH 6.0 Phosphate Buffer (see pH (791)), and dissolve in it 100 mg of sodium bisulfite.

Acid-washed solvent hexane—To 100 mL of solvent hexane contained in a separator add 10 mL of sulfuric acid, shake for not less than 12 hours, and allow the layers to separate. Transfer the acid-washed solvent to a distilling flask, and distill slowly, retaining only that portion distilling between 35 ° and 50 °. Use only freshly distilled material.

Disisopropyl ether—Place 100 mL of disisopropyl ether in a distilling flask, and distill, retaining only that portion distilling between 68 ° and 69 °. Use only freshly distilled material. [Caution—Do not evaporate to the point of near-dryness, since disisopropyl ether tends to form explosive peroxides.]

Solvent hexane-disisopropyl ether mixture (mobile solvent)—Mix 50 mL of Disisopropyl ether with 50 mL of Acid-washed solvent hexane.

Chromatographic tube—Insert a small plug of glass wool at the juncture of the tube and the stem of a 600- × 13-mm chromatographic tube.

Chromatographic column—Mix 20 g of Adsorbent with 20 mL of Standard buffer solution. Make into a slurry by mixing with 100 mL of chloroform. Transfer successive portions of the slurry into the Chromatographic tube, packing firmly and evenly with a close-fitting, ground-glass tamper after each addition. Keep a layer of liquid above the packed column to prevent the formation of air spaces. Wash the column free from chloroform with Solvent hexane-disisopropyl ether mixture, and allow the solvent to fall to the level of the Adsorbent.

Procedure—Place about 250 mg of Dipmer caprol, accurately weighed and demonstrated to be free from hydrogen sulfide as directed in the Assay, in a 5-mL volumetric flask, add Solvent hexane-disisopropyl ether mixture to volume, and mix. Transfer 2.0 mL of the resulting solution to the prepared Chromatographic column. When the liquid has passed into the column, wash the wall of the tube with a 2-mL portion of Solvent hexane-disisopropyl ether mixture, and allow the washing to fall to the level of the Adsorbent. Fill the Chromatographic tube with solvent, and collect two successive fractions: (A) a 20-mL fraction containing all of the 1,2,3-trimer captopropane, and (B) a 3-mL fraction that serves as a check on the separation. To each fraction add an equal volume of alcohol, and titrate with 0.1 N iodine VS until a permanent yellow color is produced. Perform a blank titration on 20 mL of the solvent mixture that has been passed through the column prior to introduction of the test specimen, and make any necessary y correction. Fraction (B) does