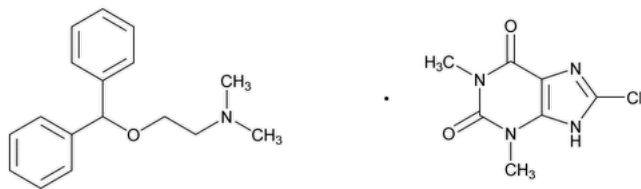


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Dimenhydrinate



$C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$ 469.96
1*H*-Purine-2,6-dione, 8-chloro-3,7-dihydro-1,3-dimethyl-, compd. with 2-(diphenylmethoxy)-*N,N*-dimethylethanamine (1:1);
8-Chlorotheophylline, compound with 2-(diphenylmethoxy)-*N,N*-dimethylethylamine (1:1) CAS RN®: 523-87-5; UNII: JB937PER5C.

DEFINITION
Dimenhydrinate contains NLT 53.0% and NMT 55.5% of diphenhydramine ($C_{17}H_{21}NO$) and NLT 44.0% and NMT 47.0% of 8-chlorotheophylline ($C_7H_7ClN_4O_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197K ▲ or 197A ▲ (USP 1-May-2021)

Add the following:

- ▲ **B.** The retention time of the diphenhydramine peak in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay, [Procedure 1: Diphenhydramine](#). ▲ (USP 1-May-2021)

Add the following:

- ▲ **C.** The retention time of the 8-chlorotheophylline peak in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay, [Procedure 2: 8-Chlorotheophylline](#). ▲ (USP 1-May-2021)

ASSAY

Change to read:

- ▲ **PROCEDURE 1:** ▲ (USP 1-MAY-2021) **DIPHENHYDRAMINE**
▲ **Solution A:** 10.0 g/L (equivalent to 13.8 mL/L) of [triethylamine](#) in [water](#); adjusted with [phosphoric acid](#) to a pH of 2.5
Solution B: [Acetonitrile](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	82	18	1.2
2	82	18	1.2
15	50	50	1.2
20	20	80	2.0
32	20	80	2.0

Return to original conditions, and re-equilibrate the system for NLT 10 min.

Diluent: [Acetonitrile](#) and [water](#) (18:82)
System suitability solution: 0.114 mg/mL of [USP Diphenhydramine Hydrochloride RS](#) and 0.1 mg/mL each of [USP Diphenhydramine Related Compound A RS](#), [USP Theophylline RS](#), and [USP Dimenhydrinate Related Compound E RS](#) in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.05 mg/mL of [USP Diphenhydramine Hydrochloride RS](#) in *Diluent*

Sample solution: 0.1 mg/mL of Dimenhydrinate in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Column temperature: 30°

Flow rate: See [Table 1](#).

Injection volume: 10 μL

System suitability

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

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between diphenhydramine related compound A and diphenhydramine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of diphenhydramine ($C_{17}H_{21}NO$) in the portion of Dimenhydrinate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

C_S = concentration of [USP Diphenhydramine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of diphenhydramine, 255.36

M_{r2} = molecular weight of diphenhydramine hydrochloride, 291.82

▲ (USP 1-May-2021)

Acceptance criteria: 53.0%–55.5% on the dried basis

Change to read:

• ▲ **PROCEDURE 2:** ▲ (USP 1-May-2021) **8-CHLOROTHEOPHYLLINE**

▲ **Solution A, Solution B, Mobile phase, Diluent, Sample solution, and Chromatographic system:** Proceed as directed in the Assay, *Procedure 1: Diphenhydramine*.

Standard solution: 0.05 mg/mL of [USP 8-Chlorotheophylline RS](#) in *Diluent*

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of 8-chlorotheophylline ($C_7H_7ClN_4O_2$) in the portion of Dimenhydrinate taken:

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

r_U = peak response of 8-chlorotheophylline from the *Sample solution*

r_S = peak response of 8-chlorotheophylline from the *Standard solution*

C_S = concentration of [USP 8-Chlorotheophylline RS](#) in the *Standard solution* (mg/mL)

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

▲ (USP 1-May-2021)

Acceptance criteria: 44.0%–47.0% on the dried basis