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Diphenhydramine Hydrochloride Oral Solution

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-diphenhydramine-hcl-os-20211029.

DEFINITION

Diphenhydramine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **Procedure**

Solution A: 11.24 g/L of sodium perchlorate monohydrate in water. Add 1 mL of trifluoroacetic acid to each L of solution prepared.

Solution B: Acetonitrile and trifluoroacetic acid (1000:1)

Solution C: *Solution A* and *Solution B* (82:18)

Solution D: *Solution A* and *Solution B* (50:50)

Mobile phase:

See *Table 1*.

Table 1

Time (min)	Solution C (%)	Solution D (%)
0	100	0
14.0	0	100
20.0	0	100
20.1	100	0
25.0	100	0

Diluent: Acetonitrile and water (18:82)

Standard stock solution: 1.0 mg/mL of USP Diphenhydramine Hydrochloride RS in *Diluent*

Standard solution: 0.25 mg/mL of USP Diphenhydramine Hydrochloride RS from the *Standard stock solution*

System suitability stock solution: 0.0125 mg/mL of USP Diphenhydramine Related Compound A RS prepared as follows. Transfer an appropriate amount of the Reference Standard to a volumetric flask. Add 5% of the flask volume of acetonitrile and dilute with *Diluent* to volume. Dilute this solution (1 in 10) with *Diluent*.

System suitability solution: 0.25 mg/mL of USP Diphenhydramine Hydrochloride RS and 0.00025 mg/mL of USP Diphenhydramine Related Compound A RS in *Diluent* from the *Standard stock solution* and *System suitability stock solution*, respectively

Sample solution: Nominally 0.25 mg/mL of diphenhydramine hydrochloride from a suitable volume of Oral Solution in *Diluent*. Pass a portion of the resulting solution through a suitable filter of 0.45-µm pore size, discarding the first few mL of filtrate. Use the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm. For *Identification A*, use a diode-array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE— ▲The relative retention times for diphenhydramine related compound A and diphenhydramine are 0.96 and 1.0, respectively.▲ (RB 1-Nov-2021)]

Suitability requirements

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

Tailing factor: 0.5–2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) in the portion of Oral Solution taken:

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

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 = nominal concentration of diphenhydramine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **ALCOHOL DETERMINATION ⟨611⟩** (if present)**:** 90.0%–110.0% of the labeled amount of ethanol (C_2H_5OH)

Delete the following:

▲▲ (RB 1-Nov-2021)

PERFORMANCE TESTS

• **DELIVERABLE VOLUME ⟨698⟩:** Meets the requirements

SPECIFIC TESTS

• **pH ⟨791⟩:** 3.5–5.5

• **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** It meets the requirements of the test for the absence of *Escherichia coli*. The total aerobic microbial count does not exceed 10^2 cfu/mL. The total yeasts and molds count does not exceed 10^1 cfu/mL.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Store at controlled room temperature.

Change to read:

• **USP REFERENCE STANDARDS ⟨11⟩**

▲▲ (RB 1-Nov-2021)

USP Diphenhydramine Hydrochloride RS

▲▲ (RB 1-Nov-2021)

USP Diphenhydramine Related Compound A RS

2-(Diphenylmethoxy)-*N*-methylethanamine hydrochloride.

$C_{16}H_{19}NO \cdot HCl$ 277.79

▲▲ (RB 1-Nov-2021)

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

Topic/Question	Contact	Expert Committee
DIPHENHYDRAMINE HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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