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Orphenadrine Citrate Injection

DEFINITION

Orphenadrine Citrate Injection is a sterile solution of Orphenadrine Citrate in Water for Injection, prepared with the aid of Sodium Hydroxide. It contains NLT 93.0% and NMT 107.0% of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$).

IDENTIFICATION

- **A.** The retention time of the major peak from the *Sample solution* corresponds to that from the *Standard solution*, as obtained in the *Assay*.
- **B.** **Identification Tests—General ⟨191⟩, *Citrate*:** Meets the requirements

ASSAY

- **Procedure**

Buffer: 5.8 g/L of monobasic ammonium phosphate in water. Adjust with ammonium hydroxide or phosphoric acid to a pH of 7.9 ± 0.05.

Mobile phase: Methanol, acetonitrile, and *Buffer* (45:15:40)

System suitability solution: 0.01 mg/mL each of USP Orphenadrine Related Compound B RS, USP Orphenadrine Related Compound C RS, USP Methylbenzhydrol RS, and 0.9 mg/mL of USP Orphenadrine Citrate RS in *Mobile phase*

Standard solution: 0.9 mg/mL of USP Orphenadrine Citrate RS in *Mobile phase*

Sample solution: Nominally 0.9 mg/mL of orphenadrine citrate from a known volume of the Injection containing NLT 90 mg of orphenadrine citrate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of orphenadrine

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between orphenadrine related compound B and orphenadrine related compound C; NLT 3.0 between orphenadrine related compound C and methylbenzhydrol

Tailing factor: NMT 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 orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) in the portion of the Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Orphenadrine Citrate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 93.0%–107.0%

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.002 mg/mL of USP Orphenadrine Citrate RS in *Mobile phase*

Sensitivity solution: 0.001 mg/mL of USP Orphenadrine Citrate RS from the *Standard solution* in *Mobile phase*

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between orphenadrine related compound B and orphenadrine related compound C; NLT 3.0 between orphenadrine related compound C and methylbenzhydrol

Tailing factor: NMT 2, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each degradation product from the *Sample solution*

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

C_S = concentration of USP Orphenadrine Citrate RS in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%, w/w)
Citric acid[a]	0.14	—	—
Orphenadrine related compound B	0.25	1.3	0.2
Orphenadrine related compound C	0.39	1.0	0.2
Methylbenzhydrol	0.51	2.4	0.2
Orphenadrine	1.0	—	—
Methyl orphenadrine[b]	1.54	1.9	0.2
Any individual unspecified degradation product	—	1.0	0.20

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%, w/w)
Total degradation products	—	—	4.0

[a] Counter ion peak; not to be reported; not to be included in total impurities.

[b] 2-(Di-*o*-tolylmethoxy)-*N*,*N*-dimethylethan-1-amine.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 5.0–6.0

• **Bacterial Endotoxins Test** ⟨85⟩**:** NMT 5.8 USP Endotoxin Units/mg of orphenadrine citrate

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Methylbenzhydrol RS

2-Methylbenzhydrol;
Also known as phenyl(*o*-tolyl)methanol.
$C_{14}H_{14}O$ 198.26

USP Orphenadrine Citrate RS

USP Orphenadrine Related Compound B RS

N-Ethyl-*N*,*N*-dimethyl [2-▲(2-▲ (ERR 1-Feb-2022) methylbenzhydryloxy)ethyl]ammonium chloride; also known as *N*-Ethyl-*N*,*N*-dimethyl-2-[phenyl(▲2▲ (ERR 1-Feb-2022) -tolyl)methoxy]ethanaminium chloride.
$C_{20}H_{28}ClNO$ 333.90

USP Orphenadrine Related Compound C RS

N-Methyl [2-(2-methylbenzhydryloxy)ethyl]amine hydrochloride; also known as *N*-methyl-2-[phenyl(*o*-tolyl)methoxy]ethanamine hydrochloride.
$C_{17}H_{21}NO \cdot HCl$ 291.82

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

Topic/Question	Contact	Expert Committee
ORPHENADRINE CITRATE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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