Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Feb-2022
Document Type: USP Monographs
DocId: GUID-70767DCA-5024-4057-8AF1-11EA5803C782_3_en-US
DOI: https://doi.org/10.31003/USPNF_M58905_03_01
DOI Ref: rpk89

Orphenadrine Citrate Extended-Release Tablets

DEFINITION

Orphenadrine Citrate Extended-Release Tablets contain NLT 90.0% and NMT 110.0% 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 of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 5.8 g/L of monobasic ammonium phosphate. Adjust with phosphoric acid to a pH of 3.2.

Mobile phase: Acetonitrile and *Buffer* (40:60)

System suitability solution: 0.1 mg/mL of USP Orphenadrine Citrate RS and 0.01 mg/mL each of USP Orphenadrine Related Compound B RS and USP Orphenadrine Related Compound C RS, in *Mobile phase*

Standard solution: 0.1 mg/mL of USP Orphenadrine Citrate RS

Sample stock solution: Nominally 0.5 mg/mL of orphenadrine citrate prepared as follows. Transfer a quantity of powder equivalent to NLT 100 mg of orphenadrine citrate, from finely powdered Tablets (NLT 20), to a suitable volumetric flask. Add 50% of the flask volume of *Mobile phase*. Sonicate for 5 min and shake for 15 min. Dilute with *Mobile phase* to volume. Pass through a suitable filter.

Sample solution: Nominally 0.1 mg/mL of orphenadrine citrate in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 30-cm; 10-µm L1 packing

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.2 between orphenadrine and orphenadrine related compound C; NLT 2.0 between orphenadrine citrate and orphenadrine related compound B, *System suitability solution*

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 Tablets 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 orphenadrine citrate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 900 mL, deaerated

Apparatus 2: 50 rpm

Times: 1, 2, 6, and 12 h

Buffer: 5.8 g/L of monobasic ammonium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (40:60). Adjust with phosphoric acid to a pH of 3.2 ± 0.1.

Standard stock solution: 1 mg/mL of USP Orphenadrine Citrate RS in *Mobile phase*. Sonication may be used to promote dissolution.

Standard solution 0.1 mg/mL of USP Orphenadrine Citrate RS in *Medium* from a suitable volume of *Standard stock solution* and *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first few mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis:

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved in the portion of the sample withdrawn at each time point (i) (mg/mL):

$$C_i = (r_U/r_S) \times C_S$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{C_3 \times [V - (2 \times V_S)] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{C_4 \times [V - (3 \times V_S)] + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of orphenadrine citrate in the portion of the sample withdrawn at time point (i) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	10–40
2	2	30–50
3	6	50–80
4	12	NLT 80

The percentages of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times: 1, 4, and 12 h

Standard solution: 0.02 mg/mL of USP Orphenadrine Citrate RS in *Medium*

Sample solution: Withdraw 10 mL of the solution under test from each vessel at each specified time point. Replace 10 mL of *Medium* in each vessel. Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Transfer 1.0 mL of the filtrate to a 50-mL volumetric flask, and dilute with *Medium* to volume.

Blank: *Medium*

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 210 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) in the sample withdrawn from the vessel at each time point (*i*):

$$C_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amounts (Q_i) of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at each time point *(i)*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of orphenadrine citrate in the portion of the sample withdrawn at time point (*i*) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	10–40
2	4	40–70
3	12	NLT 80

The percentages of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at the times specified conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

Solution A: 0.45 M monobasic potassium phosphate prepared as follows. Mix 6.12 g of monobasic potassium phosphate and 12 mL of 10 N sodium hydroxide. Dilute with water to 100 mL.

Acid stage medium: 0.1 N hydrochloric acid; 800 mL

Buffer stage medium: pH 7.5 phosphate buffer (add 100 mL of *Solution A* to the *Acid stage medium* after 1 h); 900 mL

Apparatus 2: 50 rpm

Times: 1 h in *Acid stage medium*; 4 and 10 h in *Buffer stage medium*. The time in the *Buffer stage medium* includes the time in the *Acid stage medium*.

Standard solution: 0.11 mg/mL of USP Orphenadrine Citrate RS in *Acid stage medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Blank: *Acid stage medium*

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 232 nm

Cell: 1 cm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) in the sample withdrawn from the vessel at each time point (*i*):

$$C_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amounts (Q_i) of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V_A \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V_B - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V_B - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of orphenadrine citrate in the portion of the sample withdrawn at time point (*i*) (mg/mL)

V_A = volume of *Acid stage medium*, 800 mL

L = label claim (mg/Tablet)

V_B = volume of *Buffer stage medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 3*.

Table 3

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	40–55
2	4	50–70
3	10	NLT 70

The percentages of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved at the times specified conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

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

Analysis

Sample: *Sample solution*

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

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

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

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

F = relative response factor for each degradation product (see *Table 4*)

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citric acid[a]	0.4	—	—
Orphenadrine related compound C	0.9	1.5	0.5
Orphenadrine citrate	1	—	—
Orphenadrine related compound B	1.3	1.3	0.5
2-Methylbenzhydrol[b]	2.1	2.1	0.5
2-Methylbenzophenone[c]	4	1.0	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any individual unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.5

[a] The peak is due to counter ion and is not to be reported or included in total degradation products.

[b] Also known as Phenyl(*o*-tolyl)methanol.

[c] Also known as Phenyl(*o*-tolyl)methanone.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, tight, light-resistant containers, and store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

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.

$C_{17}H_{22}ClNO$ 291.82

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

Topic/Question	Contact	Expert Committee
ORPHENADRINE CITRATE EXTENDED-RELEASE TABLETS	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(1)

Current DocID: GUID-70767DCA-5024-4057-8AF1-11EA5803C782_3_en-US

DOI: https://doi.org/10.31003/USPNF_M58905_03_01

DOI ref: rpk89