Loratadine Capsules

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 5 Expert Committee has revised the Loratadine Capsules monograph. The purpose of this revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

- *Dissolution Test 2* was validated using the Xterra C18 brand of column with L1 packing. The typical retention time for loratadine is about 5 min.

The Loratadine Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Robyn Fales, Senior Scientist I (240-221-2047 or rnp@usp.org).

Revision Bulletin
Official: June 1, 2022

Loratadine Capsules

DEFINITION

Loratadine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$).

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*.

● **B.** The UV spectrum of the major peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

● **Procedure**

Buffer: 1.74 g/L of potassium phosphate dibasic in water. Adjust with phosphoric acid to a pH of 7.2.

Solution A: Acetonitrile and methanol (50:50)

Mobile phase: *Solution A* and *Buffer* (75:25)

Diluent: Acetonitrile, methanol, 0.05 N hydrochloric acid, and 0.6 M potassium phosphate dibasic (26:26:40:8)

Standard solution: 0.1 mg/mL of USP Loratadine RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of loratadine in *Diluent*, prepared as follows. Transfer NLT 10 Capsules into a suitable volumetric flask. Add *Diluent* to about 50% of the total flask volume. Sonicate for about 30 min. Dilute with *Diluent* to volume. Transfer an appropriate volume of this solution into a suitable volumetric flask. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 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 times the retention time of loratadine

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 percentage of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

● **Dissolution** ⟨711⟩

Perform the test using the conditions under *Tier 1*. In the presence of cross-linking, repeat the test with new Capsules using the conditions under *Tier 2*.

▲**Test 1**▲ (RB 1-Jun-2022)

Tier 1

Solution A: 1 g/L of polysorbate 20 in 0.1 N hydrochloric acid, prepared as follows. Mix 8.5 mL of hydrochloric acid in 1 L of water. Add 1 g of polysorbate 20.

Medium: *Solution A*; 900 mL

Apparatus 2: 75 rpm with sinker

Time: 20 min

Tier 2

Solution B: 1 g/L of polysorbate 20 and 1.2 g/L of pepsin in 0.1 N hydrochloric acid, prepared as follows. Mix 8.5 mL of hydrochloric acid in 1 L of water. Add 1.0 g of polysorbate 20 and 1.16 g of pepsin.

Medium: *Solution B*; 900 mL

Apparatus 2: 75 rpm with sinker

Time: 20 min

Determine the amount of loratadine ($C_{22}H_{23}ClN_2O_2$) dissolved using the following method.

Mobile phase: Prepare as directed in the *Assay*.

Standard stock solution: 0.1 mg/mL of USP Loratadine RS, prepared as follows. Transfer an appropriate amount of USP Loratadine RS to a suitable volumetric flask. Add about 20% of the total flask volume of methanol. Sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: 0.01 mg/mL of USP Loratadine RS in *Medium*, from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6 mm × 25-cm, 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of loratadine

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 percentage of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$) dissolved:

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

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

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

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$) is dissolved.

▲Test 2

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

Medium: 0.1 N hydrochloric acid containing 0.1% polysorbate 20; 900 mL

Apparatus 2: 75 rpm, with sinkers

Time: 30 min

Buffer: 6.8 g/L of potassium phosphate monobasic in water. Adjust with phosphoric acid to a pH of 2.8.

Mobile phase: Acetonitrile and *Buffer* (50:50)

Standard solution: 0.011 mg/mL of USP Loratadine RS in *Medium*. [NOTE—A few milliliters of acetonitrile may be needed to reduce foaming.]

Sample solution: Pass a portion of solution under test through a suitable filter, discarding at least the first 3 mL.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of loratadine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.7

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of loratadine ($C_{22}H_{23}ClN_2O_2$) is dissolved. ▲ (RB 1-Jun-2022)

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

IMPURITIES

- **Organic Impurities**

Solution A: 1.36 g/L of potassium phosphate monobasic in water. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
15	60	40
30	58	42
42	58	42
50	25	75
60	25	75
65	75	25
75	75	25

Diluent: Prepare as directed in the *Assay*.

Standard stock solution: 1 mg/mL each of USP Loratadine RS and USP Loratadine Related Compound A RS in methanol

Standard solution: 0.01 mg/mL each of USP Loratadine RS and USP Loratadine Related Compound A RS in *Diluent*, from *Standard stock solution*

Sensitivity solution: 0.4 µg/mL each of USP Loratadine RS and USP Loratadine Related Compound A RS in *Diluent*, from *Standard solution*

Sample solution: Nominally 0.4 mg/mL of loratadine in *Diluent*, prepared as follows. Transfer NLT 10 Capsules into a suitable volumetric flask. Add *Diluent* to about 60% of the total flask volume. Sonicate for about 20 min. Allow to cool to room temperature, and dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 50 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[NOTE—See *Table 2* for relative retention times.]

Suitability requirements

Tailing factor: NMT 2.0 for loratadine and loratadine related compound A, *Standard solution*

Relative standard deviation: NMT 5.0% for loratadine and loratadine related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10 for loratadine and loratadine related compound A, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of loratadine related compound A in the portion of Capsules taken:

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

r_U = peak response of loratadine related compound A from the *Sample solution*

r_S = peak response of loratadine related compound A from the *Standard solution*

C_S = concentration of USP Loratadine Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified degradation product in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Loratadine related compound A	0.16	0.2
Loratadine	1.0	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0

SPECIFIC TESTS

● **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial viable count does not exceed 10^3 cfu/mL, and the total combined yeasts and molds count does not exceed 10^2 cfu/mL. It meets the requirements of the test for the absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

● **Packaging and Storage:** Store at a temperature between 20°–25°. Protect from freezing.

Add the following:

▲● **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Jun-2022)

● **USP Reference Standards** ⟨11⟩

USP Loratadine RS

USP Loratadine Related Compound A RS

8-Chloro-5,6-dihydro-11-(piperidin-4-ylidene)-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

$C_{19}H_{19}ClN_2$ 310.83

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