Desloratadine Orally DisintegratingTablets

Type of Posting	Revision Bulletin
Posting Date	30–Nov–2018
Official Date	01–Dec–2018
Expert Committee	Chemical Medicines Monographs 5
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Desloratadine Orally Disintegrating Tablets monograph.

The purpose of this revision is to widen the limit for any other individual unspecified degradation product in *Table 2* from NMT 0.20% to NMT 0.2% to accommodate the sponsor's FDA-approved specification.

The Desloratadine Orally Disintegrating Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Mary Koleck, Ph.D., Senior Scientific Liaison (301-230-7420 or mpk@usp.org).

Desloratadine Orally Disintegrating Tablets

DEFINITION

Desloratadine Orally Disintegrating Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of desloratadine ($C_{19}H_{19}ClN_2$).

IDENTIFICATION

• **A. Ultraviolet Absorption** ⟨197U⟩
Standard solution and **Sample solution:** Proceed as directed in the *Assay*.
Instrumental conditions
Mode: UV
Wavelength range: 230–330 nm
[Note—Alternatively, a diode array detector may be used in the *Assay* to obtain the spectra.]
Acceptance criteria: The UV spectrum of the *Sample solution* corresponds to that of the *Standard solution*.

• **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

• **Procedure**
Buffer: 6.8 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.
Mobile phase: Acetonitrile, methanol, and *Buffer* (28:7:65)
Diluent: Methanol and 0.1 N hydrochloric acid (40:60)
Standard solution: 0.05 mg/mL of USP Desloratadine RS in *Diluent*. Sonication may be used to aid dissolution.
Sample stock solution: Nominally 0.25 mg/mL of desloratadine, prepared as follows. Transfer 10 Tablets to a suitable volumetric flask, add water to 15% of the flask volume, and shake until the Tablets disintegrate completely. Add 75% of the flask volume of *Diluent* and sonicate for 30 min with intermittent shaking, and dilute with *Diluent* to volume. Centrifuge a portion of this solution. Use the supernatant.
Sample solution: Nominally 0.05 mg/mL of desloratadine from the *Sample stock solution* in *Diluent*; centrifugate
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 258 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 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 percentage of the labeled amount of desloratadine ($C_{19}H_{19}ClN_2$) 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 Desloratadine RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of desloratadine in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Disintegration** ⟨701⟩**:** NMT 30 s

• **Dissolution** ⟨711⟩
Medium: 0.1 N hydrochloric acid (degassed); 900 mL
Apparatus 2: 50 rpm
Time: 10 min
Buffer: 6.8 g/L of monobasic potassium phosphate
Solution A: Acetonitrile and methanol, (80:20)
Mobile phase: *Solution A* and *Buffer* (40:60)
Standard stock solution: 0.28 mg/mL of USP Desloratadine RS in methanol. Sonication may be used to aid dissolution.
Standard solution: (*L*/900) mg/mL of USP Desloratadine RS from the *Standard stock solution* in *Medium*, where *L* is the label claim (mg/Tablet)
Sample solution: Pass a portion of the solution under test through a suitable filter.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 258 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 40 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 percentage of the labeled amount of desloratadine ($C_{19}H_{19}ClN_2$) dissolved:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Desloratadine RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of desloratadine ($C_{19}H_{19}ClN_2$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**
Buffer: Add 10 mL/L of triethylamine to a 1.36 g/L solution of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 2.5.
Solution A: Methanol, acetonitrile, and *Buffer* (15:5:80)
Solution B: Acetonitrile, tetrahydrofuran, and *Buffer* (70:5:30)
Solution C: Dilute 8.5 mL of hydrochloric acid with methanol to 1 L.
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0

Table 1 *(continued)*

Time (min)	Solution A (%)	Solution B (%)
40	50	50
50	50	50
52	100	0
65	100	0

Diluent: *Solution C* and *Buffer* (30:70)
System suitability stock solution: 0.05 mg/mL each of USP Desloratadine Related Compound A RS and USP Desloratadine Related Compound F RS in methanol,
System suitability solution: 0.5 mg/mL of USP Desloratadine RS, 1.0 µg/mL each of USP Desloratadine Related Compound A RS and USP Desloratadine Related Compound F RS, prepared as follows. Transfer 50 mg of USP Desloratadine RS into a 100-mL volumetric flask, add 70 mL of *Diluent*, and sonicate to dissolve. Add 2 mL of the *System suitability stock solution* and dilute with *Diluent* to volume.
Standard solution: 0.0025 mg/mL of USP Desloratadine RS and 0.001 mg/mL of USP Desloratadine Related Compound F RS in *Diluent*
Sample solution: Nominally 0.5 mg/mL of desloratadine from NLT 40 Tablets, prepared as follows. Transfer an amount of powder to a suitable volumetric flask to obtain the nominal concentration of desloratadine. Add 70% of the flask volume of *Diluent* and sonicate for 20 min with intermittent shaking. Dilute with *Diluent* to volume. Centrifuge a portion of the solution and use the supernatant.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 25-cm; 5-µm packing L7
Column temperature: 30°
Flow rate: 1 mL/min
Injection volume: 40 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—Relative retention times are given in *Table 2*.]
Suitability requirements
Resolution: NLT 2.0 between desloratadine and desloratadine related compound A, *System suitability solution*
Tailing factor: NMT 2.0 for desloratadine and desloratadine related compound F, *Standard solution*
Relative standard deviation: NMT 10.0% desloratadine related compound F, *Standard solution*
Signal-to-noise ratio: NLT 10 for desloratadine peak, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Identify the impurities using the relative retention times given in *Table 2*.
Calculate the percentage of desloratadine related compound F in the portion of Tablets taken:

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

r_U = peak response of desloratadine related compound F from the *Sample solution*
r_S = peak response of desloratadine related compound F from the *Standard solution*
C_S = concentration of USP Desloratadine Related Compound F RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of desloratadine in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified degradation product in the portion of Tablets 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 desloratadine from the *Standard solution*
C_S = concentration of USP Desloratadine RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of desloratadine in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Compound	Relative Retention Time	Acceptance Criteria, NMT (%)
Dechloro desloratadine[a, b]	0.42	—
Desloratadine	1.00	—
Desloratadine related compound A[b]	1.09	—
Dehydro desloratadine[b, c]	1.33	—
Desloratadine related compound F	1.37	0.2
Loratadine[b, d]	1.89	—
Any other individual unspecified degradation product	—	▲0.2▲ (RB 1-Dec-2018)
Total degradation products	—	0.5

[a] 6,11-Dihydro-11-(piperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.
[b] This is a process impurity and is included in the table for identification only. This impurity is controlled in the drug substance. It is not to be reported for the drug product and should not be included in the total impurities.
[c] 8-Chloro-11-(piperidin-4-ylidene)benzo[5,6]cyclohepta[1,2-*b*]pyridine.
[d] 8-Chloro-6,11-dihydro-11-(1-ethoxycarbonylpiperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Desloratadine RS
  USP Desloratadine Related Compound A RS
  8-Bromo-6,11-dihydro-11-(piperidin-4-ylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.
  $C_{19}H_{19}BrN_2$ 355.27
  USP Desloratadine Related Compound F RS
  8-Chloro-6,11-dihydro-11-(*N*-formyl-4-piperidinylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.
  $C_{20}H_{19}ClN_2O$ 338.83