Almotriptan Tablets

Type of Posting	Revision Bulletin
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Expert Committee	Chemical Medicines Monographs 4
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 4 Expert Committee has revised the Almotriptan Tablets monograph. The purpose for the revision is to add *Dissolution Test* 2 to accommodate drug products which were approved with different dissolution conditions and acceptance criteria. A *Labeling* section was also added.

The Almotriptan Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated into the *Second Supplement* to *USP 40–NF 35*.

Should you have any questions, please contact Heather Joyce, Ph.D., Senior Scientific Liaison (301–998–6792 or hrj@usp.org).

Almotriptan Tablets

DEFINITION

Almotriptan Tablets contain an amount of almotriptan malate ($C_{17}H_{25}N_3O_2S \cdot C_4H_6O_5$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of almotriptan ($C_{17}H_{25}N_3O_2S$).

IDENTIFICATION

- **A. INFRARED ABSORPTION ⟨197F⟩**

  Sample: Sonicate 5 powdered Tablets in 25 mL of water. Extract the suspension with 25 mL of methylene chloride, and discard the organic phase. Add another 25 mL of methylene chloride and 3 mL of 1 N sodium hydroxide. Extract the precipitated base into the organic layer. Dry with anhydrous sodium sulfate, and evaporate the organic solvent. Prepare the residue oil as a film on a sodium chloride pellet.

  Acceptance criteria: The IR spectrum obtained from the *Sample* is consistent with that of similarly prepared USP Almotriptan Malate RS.

- **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**

  Protect samples, the Reference Standards, and solutions containing them from light.

  Buffer: Add 10 mL of triethylamine to every 1000 mL of 0.01 M phosphoric acid. Adjust with phosphoric acid to a pH of 6.0.

  Mobile phase: Acetonitrile and *Buffer* (10:90)

  Standard solution: 0.5 mg/mL of USP Almotriptan Malate RS in *Mobile phase*. Sonication may be used to aid in dissolution.

  System suitability stock solution: 0.1 mg/mL each of USP Almotriptan Related Compound B RS, USP Almotriptan Related Compound C RS, and USP Almotriptan Related Compound D RS in methanol. Sonication may be used to aid in dissolution.

  System suitability solution: 0.001 mg/mL each of USP Almotriptan Related Compound B RS, USP Almotriptan Related Compound C RS, and USP Almotriptan Related Compound D RS prepared from the *System suitability stock solution* in *Standard solution*

  Sample solution: Nominally 0.5 mg/mL of almotriptan from Tablets prepared as follows. Transfer NLT 8 Tablets into a suitable volumetric flask, and add 80% of the flask volume of *Mobile phase*. Sonicate for NLT 10 min, and dilute with *Mobile phase* to volume. Stir for 30 min, and centrifuge. Pass a portion of the supernatant through a suitable filter of 0.45-µm pore size. Use the filtrate.

  Chromatographic system

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

  Mode: LC

  Detector: UV 210 nm

  Column: 2.1-mm × 10-cm; 1.8-µm packing L1

  Column temperature: 40°

  Flow rate: 0.55 mL/min

  Injection volume: 3 µL

  System suitability

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

  [NOTE—See *Table 1* for the relative retention times.]

  Suitability requirements

  Resolution: NLT 1.5 between almotriptan related compound C and almotriptan peaks, *System suitability solution*

  Tailing factor: NMT 3.0, *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 almotriptan ($C_{17}H_{25}N_3O_2S$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

  M_{r1} = molecular weight of almotriptan, 335.46

  M_{r2} = molecular weight of almotriptan malate, 469.55

  Acceptance criteria: 90.0%–110.0% of the labeled amount of almotriptan

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION ⟨711⟩**

  Test 1 (RB 1-Feb-2017)

  Medium: 0.1 N hydrochloric acid; 900 mL

  Apparatus 2: 50 rpm

  Time: 15 min

  Standard solution: (*L*/600) mg/mL of USP Almotriptan Malate RS in *Medium,* where *L* is the label claim in mg/Tablet

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

  Instrumental conditions

  Mode: UV

  Analytical wavelength

  For Tablets labeled to contain 6.25 mg: 228 nm

  For Tablets labeled to contain 12.5 mg: 284 nm

  Blank: *Medium*

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of almotriptan ($C_{17}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

  A_U = absorbance of the *Sample solution*

  A_S = absorbance of the *Standard solution*

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

  L = label claim (mg/Tablet)

  V = volume of *Medium,* 900 mL

  M_{r1} = molecular weight of almotriptan, 335.46

  M_{r2} = molecular weight of almotriptan malate, 469.55

  Tolerances: NLT 80% (*Q*) of the labeled amount of almotriptan ($C_{17}H_{25}N_3O_2S$) 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; 900 mL

  Apparatus 2: 50 rpm

  Time: 30 min

  Standard stock solution: 0.425 mg/mL of USP Almotriptan Malate RS, equivalent to 0.30 mg/mL of almotriptan, in water

Standard solution: 0.021 mg/mL of USP Almotriptan Malate RS, equivalent to 0.015 mg/mL of almotriptan, from the *Standard stock solution* in *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 5 mL. Use the remaining filtrate.
Instrumental conditions
(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)
Mode: UV
Analytical wavelength: 283 nm
Blank: *Medium*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of almotriptan ($C_{17}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Almotriptan Malate RS in the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium,* 900 mL
M_{r1} = molecular weight of almotriptan, 335.46
M_{r2} = molecular weight of almotriptan malate, 469.55

Tolerances: NLT 80% (*Q*) of the labeled amount of almotriptan ($C_{17}H_{25}N_3O_2S$) is dissolved. ● (RB 1-Feb-2017)

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

IMPURITIES

- **Organic Impurities**

Mobile phase, Standard solution, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Samples: *Standard solution*, *System suitability solution*, and *Sample solution*
Chromatograph the *System suitability solution* and identify the components on the basis of their relative retention times, as shown in *Table 1*.
Calculate the percentage of each degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each degradation product from the *Sample solution*
r_S = peak response of almotriptan from the *Standard solution*
C_S = concentration of USP Almotriptan Malate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of almotriptan in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of almotriptan, 335.46
M_{r2} = molecular weight of almotriptan malate, 469.55

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Spiroalmotriptan[a]	0.32	0.4
2-Hydroxyalmotriptan[b]	0.47	0.2
Almotriptan related compound B[c]	0.82	—
Almotriptan related compound C[c]	0.93	—
Almotriptan	1.0	—
Almotriptan related compound D	1.39	0.2
Any individual unspecified degradation product	—	0.2
Total degradation products	—	1.0

[a] 1′-Methyl-5-[(pyrrolidin-1-ylsulfonyl)methyl]spiro[indoline-3,3′-pyrrolidin]-2-ol.
[b] 3-[2-(Dimethylamino)ethyl]-5-[(pyrrolidin-1-ylsulfonyl)methyl]-1*H*-indol-2-ol.
[c] This is a process impurity that is included in this table for identification only. This impurity is controlled in the drug substance. This impurity is not to be reported for the drug product and is not to be included in the total degradation products.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

Add the following:

●• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.● (RB 1-Feb-2017)

- **USP Reference Standards** ⟨**11**⟩
USP Almotriptan Malate RS
USP Almotriptan Related Compound B RS
2-{5-[(Pyrrolidin-1-ylsulfonyl)methyl]-1*H*-indol-3-yl}ethanamine hemifumarate.
$C_{15}H_{22}N_3O_2S \cdot {}^1/_2C_4H_4O$ 365.46
USP Almotriptan Related Compound C RS
N-Methyl-2-{5-[(pyrrolidin-1-ylsulfonyl)methyl]-1*H*-indol-3-yl}ethanamine.
$C_{16}H_{23}N_3O_2S$ 321.44
USP Almotriptan Related Compound D RS
1-[({3-[2-(Dimethylamino)ethyl]indol-5-yl}methyl) sulfonyl]pyrrolidine *N*-oxide.
$C_{17}H_{25}N_3O_3S$ 351.46