

BRIEFING

Almotriptan Tablets. This monograph was posted on the USP Website as a draft USP Pending Monograph for public comment on November 30, 2009. No comments were received. The Monograph Development—Psychiatrics and Psychoactives Expert Committee has approved the monograph as an Authorized USP Pending Monograph.

The liquid chromatographic procedure in the test for *Organic Impurities* and in the *Assay* is based on analyses performed with the Phenomenex Gemini or Waters XTerra RP 18 brand of L1 column. The typical retention time for the almotriptan peak is 6.3 min for both *Organic Impurities* and the *Assay*.

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Almotriptan Tablets

v. 1 Authorized May 1, 2010

DEFINITION

Almotriptan Tablets contain NLT 90.0% and NMT 110.0% of $C_{17}H_{25}N_3O_2S$.

IDENTIFICATION

• **A. ULTRAVIOLET ABSORPTION** (197U)

Wavelength range: 200–320 nm

Sample solution: 12.4 µg/mL of almotriptan malate in 0.1 N hydrochloric acid from the *Sample solution* in the *Assay*

- **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: 3.5 g/L of citric acid. Adjust with 10 N sodium hydroxide to a pH of 3.6.

Mobile phase: Acetonitrile and *Buffer* (1:4)

System suitability solution: Use the *Standard solution*, prepared as directed in the test for *Organic Impurities*.

Standard solution: 0.43 mg/mL of USP Almotriptan Malate RS in *Buffer*

Sample solution: 0.31 mg/mL of almotriptan malate prepared as follows: Transfer NLT 5 Tablets to a suitable volumetric flask. Add 0.1 N hydrochloric acid to fill 30% of the final volume, and sonicate to disintegrate the Tablets. Dilute with *Buffer* to volume, and stir for 30 min. Pass a portion through a filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 283 nm

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

Temperature: 30°

Flow rate: 1.5 mL/min

Injection size: 10 µL

Run time: 2 times the retention time of the almotriptan peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between almotriptan malate and almotriptan related compound A, *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 $C_{17}H_{25}N_3O_2S$ 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 the *Sample solution*
 - r_S = peak response of the *Standard solution*
 - C_S = concentration of almotriptan malate in the *Standard solution* (mg/mL)
 - C_U = nominal concentration of almotriptan in the *Sample solution* (mg/mL)
 - M_{r1} = molecular weight of almotriptan, 335.47
 - M_{r2} = molecular weight of almotriptan malate, 469.56
- Acceptance criteria:** 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION** (711)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: 22 µg/mL of USP Almotriptan Malate RS in *Medium*

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

Detector: UV 283 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of almotriptan dissolved:

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

- A_U = absorbance of the *Sample solution*
- A_S = absorbance of the *Standard solution*
- C_S = concentration of the *Standard solution* (mg/mL)
- L = Tablet label claim (mg)
- M_{r1} = molecular weight of almotriptan, 335.47
- M_{r2} = molecular weight of almotriptan malate, 469.56
- V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of almotriptan is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

Buffer and Mobile phase: Proceed as directed in the *Assay*.

Standard solution: 13 µg/mL each of USP Almotriptan Malate and USP Almotriptan Related Compound A in *Buffer*

Sample solution: Proceed as directed in the *Assay*.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

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

Temperature: 30°

Flow rate: 1.5 mL/min

Injection size: 10 µL

Run time: 7 times the retention time of the almotriptan peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between almotriptan and almotriptan related compound A

Relative standard deviation: NMT 10.0% for the almotriptan peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity 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 individual impurity 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

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

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%. [NOTE—The malic acid peak is not included in total impurities.]

• **USP REFERENCE STANDARDS** (11)

USP Almotriptan Malate RS

USP Almotriptan Related Compound A RS

[(3-(2-(Dimethylamino)ethyl)-5-(((pyrrolidin-1-yl)sulfonyl)methyl)-1*H*-indol-1-yl)methanol]
($C_{18}H_{27}N_3O_3S$ 365.49)

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Malic acid	0.3	—
Almotriptan related compound A ^a	0.9	—
Almotriptan malate	1.0	—
Any other individual impurity	—	0.20

^a (3-(2-(Dimethylamino)ethyl)-5-(((pyrrolidin-1-yl)sulfonyl)methyl)-1*H*-indol-1-yl)methanol.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and stored at controlled room temperature.