

BRIEFING

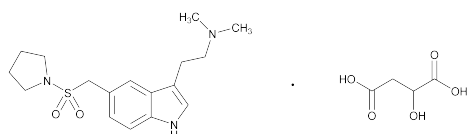
Almotriptan Malate. This monograph was posted on the USP Website as a draft USP Pending Monograph for public comment on November 30, 2009. No comments were received. The Monograph Development—Psychiatrics and Psychoactives Expert Committee has approved the monograph as an Authorized USP Pending Monograph.

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 Malate

v. 1 Authorized May 1, 2010



$C_{17}H_{25}N_3O_2S \cdot C_4H_6O_5$ 469.55
 1-[[[3-[2-(Dimethylamino)ethyl]-1H-indol-5-yl]methyl]sulfonyl]pyrrolidine, hydroxybutanedioate (1:1);
 1-[[[3-[2-(Dimethylamino)ethyl]indol-5-yl]methyl]sulfonyl]pyrrolidine malate (1:1) [181183-52-8].

DEFINITION

Almotriptan Malate contains NLT 98.0% and NMT 102.0% of $C_{17}H_{25}N_3O_2S \cdot C_4H_6O_5$, calculated on the dried basis.

IDENTIFICATION

- A. INFRARED ABSORPTION (197K)**
- 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*. [NOTE—Sonicate, if necessary.]
Sample solution: 0.43 mg/mL of Almotriptan Malate in *Buffer*. [NOTE—Sonicate, if necessary.]
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 $C_{17}H_{25}N_3O_2S \cdot C_4H_6O_5$ in the portion of Almotriptan Malate taken:

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

r_U = peak response of the *Sample solution*
 r_S = peak response of the *Standard solution*
 C_S = concentration of USP Almotriptan Malate RS from the *Standard solution* (mg/mL)
 C_U = concentration of Almotriptan Malate from the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities

• **RESIDUE ON IGNITION (281):** NMT 0.1%

Organic Impurities

• **PROCEDURE**

Buffer and Mobile phase: Proceed as directed in the *Assay*.
Standard solution: 13 μg/mL each of USP Almotriptan Malate RS and USP Almotriptan Related Compound A RS in *Buffer*. [NOTE—Sonicate, if necessary.]
Sample solution: 1.4 mg/mL of Almotriptan Malate in *Buffer*. [NOTE—Sonicate, if necessary.]

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 the almotriptan malate and almotriptan related compound A peaks
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 Almotriptan Malate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

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* (μg/mL)
 C_U = concentration of Almotriptan Malate in the *Sample solution* (μg/mL)
 F = relative response factor (see *Impurity Table 1*)
 M_{r1} = molecular weight of almotriptan, 335.46
 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 the total impurities.]

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Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Malic acid	0.3	—	—
Almotriptan hydrazine precursor ^a	0.7	0.11	0.1
Almotriptan related compound A ^b	0.9	0.88	0.1
Almotriptan triptamine ^c	0.92	0.8	0.1
Almotriptan malate	1.0	—	—
Almotriptan <i>N</i> -oxide ^d	1.4	0.9	0.1
Almotriptan aniline precursor ^e	1.8	0.15	0.1
Any other individual impurity	—	1.0	0.10

^a 1-(4-Hydrazinylbenzylsulfonyl)pyrrolidine.

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

^c 2-{5-[(Pyrrolidin-1-ylsulfonyl)methyl]-1*H*-indol-3-yl}ethanamine.

^d 1-[[{3-[2-(Dimethylamino)ethyl]indol-5-yl)methyl}sulfonyl]pyrrolidine *N*-oxide.

^e 1-(4-Aminobenzylsulfonyl) pyrrolidine.

SPECIFIC TESTS

- **Loss on Drying (731):** Dry a sample in vacuum at 105 ° for 3 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **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]
(C₁₈H₂₇N₃O₃S 365.49)