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Montelukast Sodium Oral Granules

DEFINITION

Montelukast Sodium Oral Granules contain Montelukast Sodium equivalent to NLT 90.0% and NMT 108.0% of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$).

[NOTE—Avoid exposure of samples containing montelukast to light.]

IDENTIFICATION

• **A. SPECTROSCOPIC IDENTIFICATION TESTS** (197), *Ultraviolet-Visible Spectroscopy*: **197U**

Diluent: Methanol and [water](#) (3:1)
Standard solution: 3.3 µg/mL of [USP Montelukast Dicyclohexylamine RS](#) in *Diluent*
Sample stock solution: Nominally 0.02 mg/mL of montelukast prepared as follows. Transfer the contents of one packet to a suitable volumetric flask, add 66% of the flask volume of *Diluent*, shake well, and sonicate for 15 min with occasional shaking. Cool to room temperature, dilute with *Diluent* to volume, and mix well.

Sample solution: Nominally 2 µg/mL of montelukast in *Diluent* from the *Sample stock solution*. Pass a portion of the resulting solution through a suitable filter of 0.45-µm pore size or centrifuge to obtain a clear solution.

Wavelength range: 210–400 nm
Acceptance criteria: The *Sample solution* exhibits maxima only at the same wavelengths as 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**

Diluent: Methanol and [water](#) (3:1)
Solution A: 0.2% (v/v) [trifluoroacetic acid](#) in [water](#)
Solution B: Methanol and acetonitrile (3:2)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	48	52
5	45	55
12	45	55
22	25	75
23	25	75
25	48	52
30	48	52

Standard solution: 0.33 mg/mL of [USP Montelukast Dicyclohexylamine RS](#) in *Diluent*
System suitability solution: Transfer 10 mL of the *Standard solution* to a clear 10-mL volumetric flask, add 4 µL of [hydrogen peroxide](#), and mix well. Expose the flask for at least 4 h to ambient light or 10 min to a 4 klx cool white light. [NOTE—Montelukast is partially converted to the *cis*-isomer under these conditions.]
Sensitivity solution: 0.33 µg/mL of [USP Montelukast Dicyclohexylamine RS](#) in *Diluent* from the *Standard solution*
Sample solution: Nominally 0.24 mg/mL of montelukast prepared as follows. Transfer the equivalent of 60 mg of montelukast from the contents of the packets (NLT 15) to a 500-mL volumetric flask, and add 250 mL of *Diluent*. Shake well and sonicate for 30 min.

occasional shaking. Pass a portion of the resulting solution through a suitable filter of 0.45-μm pore size or centrifuge to obtain a clear solution.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 255 nm

Columns

Guard: 3.0-mm × 4-mm; packing [L11](#)

Analytical: 4.6-mm × 10-cm; 3-μm packing [L11](#)

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

Run time: 2 times the retention time of montelukast

System suitability

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

[NOTE—The relative retention times for the *cis*-isomer and montelukast are about 0.92 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the *cis*-isomer and montelukast, *System suitability solution*

Relative standard deviation: NMT 2.0% for five injections, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$) in the portion of Oral Granules taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Montelukast Dicyclohexylamine RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of montelukast, 586.18

M_{r2} = molecular weight of montelukast dicyclohexylamine, 767.50

Acceptance criteria: 90.0%–108.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: 0.5% (w/v) [sodium dodecyl sulfate](#) in [water](#); 900 mL. Do not deaerate.

Apparatus 1: 100 mesh; 50 rpm

Time: 15 min

Solution A: 0.2% (v/v) [trifluoroacetic acid](#) in [water](#)

Solution B: 0.2% (v/v) [trifluoroacetic acid](#) in acetonitrile

Mobile phase: *Solution A* and *Solution B* (1:1)

Standard stock solution: 0.33 mg/mL of [USP Montelukast Dicyclohexylamine RS](#) in methanol (equivalent to 0.25 mg/mL of montelukast)

Standard solution: ($L/900$) mg/mL of montelukast in *Medium* from the *Standard stock solution*, where L is the label claim in mg/packet of montelukast

Sample solution: Place the entire contents of one packet in the basket. At the appropriate time point, pass a portion of the solution under test through a suitable filter to obtain a clear solution. Discard the first 10 mL of the filtrate.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 389 nm

Column: 3.0-mm × 10-cm; 5-μm packing [L11](#)

Column temperature: 50°

Flow rate: 0.9 mL/min

Injection volume: 25 μL

Run time: 1.5 times the retention time of montelukast

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$) dissolved:

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

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

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

C_S = concentration of montelukast in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/packet)

Tolerances: NLT 85% (Q) of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$) is dissolved.

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

Medium: 0.5% (w/v) [sodium dodecyl sulfate](#) in [water](#); 900 mL

Apparatus 1: 100 mesh; 50 rpm

Time: 15 min

Solution A: 0.07 g/L of [monobasic sodium phosphate](#)

Solution B: Acetonitrile

Mobile phase: *Solution A* and *Solution B* (45:55). Add 1.33 mL/L of triethylamine and adjust with phosphoric acid to a pH of 6.7.

Standard stock solution: 0.1 mg/mL of montelukast from montelukast sodium hydrate prepared as follows. Transfer a suitable amount of montelukast sodium hydrate to an appropriate volumetric flask. Dissolve in 4% of the flask volume of methanol and dilute with *Medium* to volume. Determine the water content of montelukast sodium hydrate at the time of use.

Standard solution: 0.004 mg/mL of montelukast in *Medium* from the *Standard stock solution*

Sample solution: Place the entire contents of one packet in the basket. At the appropriate time point, centrifuge a portion of the solution under test.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 5-cm; 1.8-μm packing [L1](#)

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 100 μL

Run time: 1.5 times the retention time of montelukast

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$) 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 montelukast in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/packet)

Tolerances: NLT 80% (Q) of the labeled amount of montelukast ($C_{35}H_{36}ClNO_3S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.



Documents

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