Telmisartan Tablets

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Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Telmisartan Tablets. The purpose for the revision is to add *Dissolution Test 3* to accommodate the FDA approved drug products with different dissolution conditions and tolerance than the currently official dissolution tests.

Additionally, the relative retention times for telmisartan and telmisartan related compound A were added in the *Assay* section.

The Telmisartan Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in the *Second Supplement* to *USP 41–NF 36*.

Should you have any questions, please contact Sujatha Ramakrishna, Scientific Liaison (301-816-8349 or sxr@usp.org).

Telmisartan Tablets

DEFINITION

Telmisartan Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of telmisartan ($C_{33}H_{30}N_4O_2$).

IDENTIFICATION

- **A. ULTRAVIOLET ABSORPTION ⟨197U⟩:** The spectrum of the solution under test corresponds to that of the *Standard solution*, as obtained in *Dissolution Test 1*.
- **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

Change to read:

- **PROCEDURE**

Diluent: 0.005 N methanolic solution of sodium hydroxide

Buffer: 2.0 g/L of ammonium dihydrogen phosphate. Adjust with 1 M phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (70:30)

Standard stock solution: 0.8 mg/mL of USP Telmisartan RS and 0.1 mg/mL of USP Telmisartan Related Compound A RS in *Diluent*

Standard solution: 0.11 mg/mL of USP Telmisartan RS and 0.013 mg/mL of USP Telmisartan Related Compound A RS in *Mobile phase* from the *Standard stock solution*. Pass the solution through a membrane filter of 0.45-µm pore size.

Sample solution: Transfer NLT 20 Tablets into a suitable volumetric flask, and add about 80% of the volume of *Diluent*. Swirl to disperse, and sonicate for about 10 min. Allow to cool to room temperature, dilute with *Diluent* to volume, and mix. Pass the resulting solution through a membrane filter of 0.45-µm pore size. Further dilute quantitatively in *Mobile phase* to prepare a solution having a concentration of 0.11 mg/mL.

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 298 nm
Column: 4.0-mm × 4-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 0.7 mL/min
Injection volume: 5 µL

System suitability
Sample: *Standard solution*
Suitability requirements
●[NOTE—The relative retention times for telmisartan related compound A and telmisartan are 0.53 and 1.00, respectively.]● (RB 1-Nov-2017)
Resolution: NLT 3 between telmisartan and telmisartan related compound A
Tailing factor: NMT 2.0 for the telmisartan peak
Capacity factor: NLT 1.5
Relative standard deviation: NMT 2.0%

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of telmisartan ($C_{33}H_{30}N_4O_2$) in the portion of Tablets taken:

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

r_U = peak response of telmisartan from the *Sample solution*
r_S = peak response of telmisartan from the *Standard solution*
C_S = concentration of USP Telmisartan RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of telmisartan in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION ⟨711⟩**

Test 1
Medium: pH 7.5 phosphate buffer (prepared by dissolving 13.61 g of potassium dihydrogen phosphate in about 800 mL of water, adjusting with 2 M sodium hydroxide to a pH of 7.5, and diluting with water to 1000 mL); 900 mL
Apparatus 2: 75 rpm
Time: 30 min
Standard solution: Transfer about 44 mg of USP Telmisartan RS to a 100-mL volumetric flask. Add 1 mL of 0.1 M sodium hydroxide, and dilute with methanol to volume. Dilute this solution quantitatively with *Medium* to obtain a solution having a final concentration of about 0.011 mg/mL.
Sample solution
For Tablets labeled to contain 20 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Further dilute the filtrate with *Medium* (1:2).
For Tablets labeled to contain 40 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Further dilute the filtrate with *Medium* (1:4).
For Tablets labeled to contain 80 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Further dilute the filtrate with *Medium* (1:8).
Instrumental conditions
Mode: UV
Analytical wavelength: 296 nm
Blank: *Medium*
Analysis
Samples: *Standard solution* and *Sample solution*
Determine the percentage of telmisartan ($C_{33}H_{30}N_4O_2$) dissolved:

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

A_U = absorbance of the *Sample solution*
C_S = concentration of the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
A_S = absorbance of the *Standard solution*
D = dilution factor of the *Sample solution*
L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of telmisartan ($C_{33}H_{30}N_4O_2$) 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: 75 rpm
Time: 45 min
Buffer: 2.72 g/L of potassium dihydrogen phosphate. Add 2 mL of triethylamine per liter of solution and adjust with phosphoric acid to a pH of 2.4.
Mobile phase: Acetonitrile and *Buffer* (40:60)
Standard stock solution: 0.44 mg/mL of USP Telmisartan RS prepared as follows. To a suitable amount of

USP Telmisartan RS in a suitable volumetric flask add methanol, about 50% of the total volume. Sonicate to dissolve, cool to room temperature, and dilute with *Medium* to volume.

Standard solution: (*L*/900) mg/mL of USP Telmisartan RS in *Medium* from *Standard stock solution*, where *L* is the label claim in mg/Tablet

Sample solution: Pass portions of the solution under test through a suitable filter of 0.45-µm pore size and discard the first 3 mL of the filtrate.

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 298 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 20 µL
Run time: NLT 1.6 times the retention time of telmisartan

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 telmisartan ($C_{33}H_{30}N_4O_2$) 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 Telmisartan 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 telmisartan ($C_{33}H_{30}N_4O_2$) is dissolved.

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

Medium, Apparatus 2, and **Instrumental conditions:** Proceed as directed in *Dissolution Test 1*.

Time: 20 min

Standard solution: 0.011 mg/mL of USP Telmisartan RS prepared as follows. Transfer about 44 mg of USP Telmisartan RS to a 100-mL volumetric flask. Add 1 mL of 0.1 M sodium hydroxide, and sonicate to dissolve. Dilute with methanol to volume and mix. Dilute this solution quantitatively with *Medium* to obtain a solution of the required final concentration.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and discard the first few milliliters. Dilute quantitatively with *Medium* as needed.

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of telmisartan ($C_{33}H_{30}N_4O_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
D = dilution factor of the *Sample solution*
L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of telmisartan ($C_{33}H_{30}N_4O_2$) is dissolved.● (RB 1-Nov-2017)

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

IMPURITIES

• **Organic Impurities**
Diluent, Buffer, Mobile phase, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity from the *Sample solution*
r_S = peak response of telmisartan from the *Sample solution*

Acceptance criteria: NMT 0.2% of any individual impurity

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.
• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
• **USP Reference Standards** ⟨11⟩
USP Telmisartan RS
USP Telmisartan Related Compound A RS
1,7′-Dimethyl-2′-propyl-1*H*,3′*H*-2,5′-bibenzo[*d*]imidazole.
$C_{19}H_{20}N_4$ 304.39