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_{4}O_{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 Related Compound A 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 Diluent.
  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.] (08-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_{4}O_{2}) in the portion of Tablets taken:
    Result = \left(\frac{r_s}{r_0}\right) \times \left(\frac{C_s}{C_0}\right) \times 100
    \[r_s\] = peak response of telmisartan from the Standard solution
    \[C_s\] = concentration of USP Telmisartan RS in the Standard solution (mg/mL)
    \[C_0\] = 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 the labeled amount of telmisartan (C_{33}H_{30}N_{4}O_{2}) dissolved:
    Result = \left(\frac{A_U \times C_s \times V \times 100}{A_S \times D \times L}\right)
    \[A_U\] = 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_{4}O_{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**
**Relative standard deviation:** NMT 2.0%

**Analysis**
**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of telmisartan (C33H30N4O2) dissolved:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times C_S \times V \times \left( \frac{1}{L} \right) \times 100
\]

where
- \(r_U\) = 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 (C33H30N4O2) is dissolved.

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

**IMPUERITIES**
**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:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times 100
\]

where
- \(r_U\) = 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 indicates that no additional test is required. 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.