In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Tadalafil Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution test. In addition, Apparatus 2 in *Dissolution Test 1* is revised to indicate that suitable sinkers may be used if necessary. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

* Dissolution Test 2 was validated using a Zorbax SB brand of L7 column. The typical retention time for tadalafil is about 2.0 min.

The Tadalafil Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Senior Scientific Liaison (301-998-6818 or rhy@usp.org).
Tadalafil Tablets

**DEFINITION**
Tadalafil Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of tadalafil (C_{22}H_{19}N_{3}O_{7}).

**IDENTIFICATION**

- **A. INFRARED ABSORPTION** (197)
  
  [Note—Methods described in Infrared Absorption (197K), or (197D) may be used.]

- **B. RETENTION TIME**
  
  [Note—The retention time of the major peak of the Standard solution of Tadalafil (C_{22}H_{19}N_{3}O_{7}) in the portion of Tablets taken:
  
  \[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_i}{C_o} \right) \times 100 \]
  
  \( r_U \) = peak response from the Sample solution
  \( r_S \) = peak response from the Standard solution
  \( C_i \) = concentration of USP Tadalafil RS in the Standard solution (mg/mL)
  \( C_o \) = nominal concentration of tadalafil in the Sample solution (mg/mL)

  Acceptance criteria: 90.0%–110.0%

  **ASSAY**

  - **PROCEDURE**
    
    Mobile phase: Acetonitrile, water, and trifluoroacetic acid (35:65:0.1)
    
    Diluent: Acetonitrile and water (1:1)
    
    Standard solution: 0.25 mg/mL of USP Tadalafil RS in Diluent
    
    System suitability solution: To partially convert tadalafil to the 6R,12αS diastereomer, transfer 25 mL of the Standard solution into a suitable container. Add 0.25 mL of 5 N sodium hydroxide, mix well, and let stand for 30 min. Neutralize the solution to pH 7 by drop-wise addition of trifluoroacetic acid. [Note—This solution is stable for 1 month when stored in a refrigerator.]
    
    Sample solution: Place NLT 20 Tablets into an appropriate size volumetric flask. Fill the flask about halfway with Diluent, and shake the mixture for about 15 min to disintegrate the Tablets. If any large fragments remain, sonicate the solution for 2 min or until fragments are dispersed. Dilute with Diluent to volume, and mix. Allow the solution to stand for at least 1 h to further aid Tablet dissolution. If necessary, shake the solution and perform a secondary dilution to obtain a final nominal concentration of 0.25 mg/mL. Centrifuge or filter the solution. [Note—The initial concentration before a secondary dilution step should not exceed 6 mg/mL.]
    
    Chromatographic system
    
    (See Chromatography (621), System Suitability.)
    
    Mode: LC
    
    Detector: UV 225 nm
    
    Column: 4.6-mm × 15-cm; 3.5-µm packing L7
    
    Column temperature: 35°
    
    Flow rate: 1.0 mL/min
    
    Injection volume: 10 µL

  - **DILUTION** (711)
    
    "No Test" (88:5-Nov-2019)
    
    Medium: 0.5% sodium dodecyl sulfate; 1000 mL
    
    
    Times: 10 and 30 min
    
    Mobile phase: Methanol and water (50:50)
    
    Standard stock solution: 0.25 mg/mL of USP Tadalafil RS in acetonitrile and water (1:1)
    
    Sample solution: Pass a portion of the solution under test through a suitable filter.

  - **CHROMATOGRAPHIC SYSTEM**
    
    (See Chromatography (621), System Suitability.)
    
    Mode: LC
    
    Detector: UV 225 nm
    
    Column: 4.6-mm × 5.0-cm; 3.5-µm packing L7
    
    Column temperature: 40°
    
    Flow rate: 2.0 mL/min
    
    Injection volume: 50 µL

  - **SYSTEM SALTABILITY**
    
    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 tadalafil (C_{22}H_{19}N_{3}O_{7}) dissolved at each time point (Q):
    
    \[ Q_{10} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_i}{L} \right) \times V \times 100 \]
    
    \[ Q_{30} = (Q_{10} \times V/V) + \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_i}{L} \right) \times (V - V) \times 100 \]

    \( r_U \) = peak response from the Sample solution
    \( r_S \) = peak response from the Standard solution
    \( C_i \) = concentration of USP Tadalafil RS in the Standard solution (mg/mL)
    \( L \) = label claim (mg/Tablet)

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If the product complies with this procedure, the NLT 80% (50 rpm, use suitable sinkers if necessary) = concentration of USP Tadalafil RS in the Standard solution (mg/mL)

\[ C_0 = \text{nominal concentration of tadalafil in the Sample solution (mg/mL)} \]

Acceptance criteria: Meet the requirements for coated Tablets

IMPURITIES

- ORGANIC IMPURITIES

Mobile phase, Diluent, Standard solution, System suitability solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Sensitivity solution: 0.25 µg/mL of USP Tadalafil RS in Diluent from the Standard solution

System suitability

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

[NOTE—The relative retention times for tadalafil and the 6R,12aS diastereomer of tadalafil are about 1.0 and 1.2, respectively.]

Suitability requirements

Tailing factor: NMT 1.5, Standard solution
Relative standard deviation: NMT 2.0%, Standard solution
Resolution: NLT 3 between tadalafil and the 6R,12aS diastereomer peak, System suitability solution
Signal-to-noise ratio: NLT 20, Sensitivity solution

Analysis

Sample: Sample solution
Calculate the percentage of each impurity in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_i}{r_f} \right) \times C_i \times \frac{V}{L} \times (1/L) \times 100 \]

Individual impurities: NMT 0.2%
Total impurities: NMT 0.3%
Reporting level for impurities: 0.05%

ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE: Preserve in tight containers. Store at controlled room temperature.

Add the following:

- Labeling: When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. [RB 1-Nov-2019]

- USP Reference Standards (11)

USP Tadalafil RS