Metyrosine Capsules

**Type of Posting**  
Revision Bulletin

**Posting Date**  
21-Sep-2020

**Official Date**  
22-Sep-2020

**Expert Committee**  
Small Molecules 2

**Reason for Revision**  
Compliance, without postponement

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 2 Expert Committee has revised the Metyrosine Capsules monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test.

Labeling information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Metyrosine Capsules monograph Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Donald Min, Senior Scientific Liaison to the Small Molecules 2 Expert Committee (301-230-7457 or [ddm@usp.org](mailto:ddm@usp.org)).
**Metyrosine Capsules**

**DEFINITION**
Metyrosine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of metyrosine (C₁₀H₁₃NO₃).

**IDENTIFICATION**
- **A. ULTRAVIOLET ABSORPTION**
  - **Sample solution:** 0.1 mg/mL solution of the Capsule contents in dilute hydrochloric acid (1 in 100)
  - **Acceptance criteria:** The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Metyrosine RS, concomitantly measured.

**ASSAY**
- **PROCEDURE**
  - **Diluent:** Dilute hydrochloric acid (1 in 100)
  - **Standard solution:** 100 µg/mL of USP Metyrosine RS in Diluent
  - **Sample stock solution:** Combine the contents of Capsules (NLT 20), and transfer the nominal equivalent of 100 mg of metyrosine to a 100-mL volumetric flask. Add 50 mL of Diluent, shake by mechanical means for 45 min, dilute with Diluent to volume, and filter.
  - **Sample solution:** Nominally 0.1 mg/mL of metyrosine, from Sample stock solution, in Diluent

**Spectrometric conditions**
- **Mode:** UV
- **Analytical wavelength:** Maximum at about 274 nm
- **Blank:** Dilute hydrochloric acid solution (1 in 100)

**Analysis**
- **Samples:** Standard solution and Sample solution
  - Calculate the percentage of the labeled amount of metyrosine (C₁₀H₁₃NO₃) in the portion of Capsules taken:

  \[
  \text{Result} = \frac{A_U}{A_S} \times \frac{C_S}{C_U} \times 100
  \]

  - \(A_U\) = absorbance of the Sample solution
  - \(A_S\) = absorbance of the Standard solution
  - \(C_S\) = concentration of USP Metyrosine RS in the Standard solution (µg/mL)
  - \(C_U\) = nominal concentration of metyrosine in the Sample solution (µg/mL)

- **Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

*Change to read:*
- **Dissolution (711)**
  - **Test 1** (RB 22-Sep-2020)
    - **Medium:** 0.1 N hydrochloric acid; 750 mL
    - **Apparatus 1:** 100 rpm
    - **Time:** 60 min
    - **Standard solution:** USP Metyrosine RS at a known concentration in Medium
**Sample solution:** Pass a portion of the solution under test through a suitable filter. Dilute with *Medium* as needed.

**Spectrometric conditions**
- **Mode:** UV
- **Analytical wavelength:** Maximum at about 274 nm

**Analysis**
- **Samples:** *Standard solution* and *Sample solution*
- **Tolerances:** NLT 75% (Q) of the labeled amount of metyrosine (C_{10}H_{13}NO_{3}) is dissolved.

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

**Tier 1**
- **Medium:** 0.1 N *hydrochloric acid* (degassed); 750 mL
- **Apparatus 1:** 100 rpm. A 20-mesh basket may be used.
- **Time:** 30 min

**Tier 2**
- **Medium:** Transfer 15.09 ± 0.1 g of *pepsin* (Activity: 371 units/mg) into a suitable container with about 8000 mL of degassed 0.1 N *hydrochloric acid*. Stir gently to dissolve it and mix well. (Final activity of pepsin in *Medium* is about 700000 units/L); 750 mL
- **Apparatus 1:** 100 rpm. A 20-mesh basket may be used
- **Time:** 30 min

**Standard solution:** 0.33 mg/mL of *USP Metyrosine RS* prepared as follows. Transfer an appropriate amount of *USP Metyrosine RS* into a suitable volumetric flask. Add *methanol* to 2%–3% of the flask volume and sonicate to disperse. Add *Medium* to about 70% of the flask volume, and sonicate to dissolve. Dilute with *Medium* to volume. [Note—*Medium* in Tier 1 or Tier 2 should be used respectively.]

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

**Instrumental conditions**
- (See *Ultraviolet-Visible Spectroscopy (857)*.)
- **Mode:** UV
- **Analytical wavelength:** 274 nm
- **Path length:** 0.2-cm
- **Blank:** *Medium*. [Note—*Medium* in Tier 1 or Tier 2 should be used respectively.]

**System suitability**
- **Sample:** *Standard solution*
- **Suitability requirements**
  - **Relative standard deviation:** NMT 2.0%

**Analysis**
- Perform the test using the conditions in Tier 1. Perform the Tier 2 test only if the Tolerances in Tier 1 can not be met because of the presence of cross-linking in the gelatin. Repeat the test with new Capsules using the conditions in Tier 2.

**Samples:** *Standard solution* and *Sample solution*
- Calculate the percentage of the labeled amount of metyrosine (C_{10}H_{13}NO_{3}) dissolved:

\[
\text{Result} = \left( \frac{A_U}{A_S} \right) \times C_S \times V \times (1/L) \times 100
\]

- \( A_U \) = absorbance from the *Sample solution*
- \( A_S \) = absorbance from the *Standard solution*
- \( C_S \) = concentration of *USP Metyrosine RS* in the *Standard solution* (mg/mL)
\[ V = \text{volume of Medium, 750 mL} \]
\[ L = \text{label claim (mg/Capsule)} \]

**Tolerances:** NLT 80% (Q) of the labeled amount of metyrosine (C_{10}H_{13}NO_{3}) is dissolved. \( \Delta \) (RB 22-Sep-2020)

**Uniformity of Dosage Units (905):** Meet the requirements

**ADDITIONAL REQUIREMENTS**

**Packaging and Storage:** Preserve in well-closed containers.

**Add the following:**

**\( \Delta \) Labeling:** When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. \( \Delta \) (RB 22-Sep-2020)

**USP Reference Standards (11):**

USP Metyrosine RS

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**Page Information:**

Not Applicable

**DocID:**

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