

## Metyrosine Capsules

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<b>Posting Date</b>	21-Sep-2020
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<b>Expert Committee</b>	Small Molecules 2
<b>Reason for Revision</b>	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 ( $C_{10}H_{13}NO_3$ ).

## 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 ( $C_{10}H_{13}NO_3$ ) in the portion of Capsules taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

$A_U$  = 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  $15.09 \pm 0.1$  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- $\mu$ m 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:

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

$A_U$  = 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)

$V$  = volume of *Medium*, 750 mL

$L$  = label claim (mg/Capsule)

**Tolerances:** NLT 80% ( $Q$ ) of the labeled amount of metyrosine ( $C_{10}H_{13}NO_3$ ) is dissolved. ▲ (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:**

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

- **USP REFERENCE STANDARDS (11).**

[USP Metyrosine RS](#)

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#### Page Information:

Not Applicable

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