Metyrosine Capsules

Type of Posting	Notice of Intent to Revise
Posting Date	31–Jul–2020
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Expert Committee	Chemical Medicines Monographs 2

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 2 Expert Committee intends to revise the Metyrosine Capsules monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 2* to the monograph.

A *Labeling* section has also been added.

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact Donald Min, Senior Scientific Liaison to the Chemical Medicines Monographs 2 Expert Committee (301-230-7457 or ddm@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.

Notice of Intent to Revise
Official: To Be Determined

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 ▲ (TBD)

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:

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

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. ▲ (TBD)

● **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. ▲ (TBD)

● **USP REFERENCE STANDARDS** ⟨11⟩

USP Metyrosine RS

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