Hydroxyurea Capsules

Type of Posting	Notice of Intent to Revise
Posting Date	29-Dec-2023
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 3

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 3 Expert Committee intends to revise the Hydroxyurea Capsules monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Hydroxyurea Capsules monograph to add *Dissolution Test 2*. Existing references to reagents and reagent names have been updated for consistency with official reagent entry names. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

In the *Acceptance criteria* for *Identification A*, the term “wavelengths” also has been updated to “wavenumbers”, because it is the preferred terminology for infrared spectroscopy comparisons.

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 Yanyin Yang, Senior Scientist II (301-692-3623 or yanyin.yang@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

Hydroxyurea Capsules

DEFINITION

Hydroxyurea Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyurea ($CH_4N_2O_2$).

IDENTIFICATION

- **A.**

Standard: Transfer 30 mg of USP Hydroxyurea RS to a suitable centrifuge tube, and add 10 mL of anhydrous methanol. Centrifuge for 3 min. Transfer 1.0 mL of the clear supernatant to a mortar containing 500 mg of potassium bromide, triturate to a homogeneous blend, dry in a vacuum desiccator at 60° for 3 h, and prepare a suitable disk.

Sample: Transfer a portion of Capsule contents, equivalent to 30 mg of hydroxyurea, to a suitable centrifuge tube, and add 10 mL of anhydrous methanol. Centrifuge for 3 min. Transfer 1.0 mL of the clear supernatant to a mortar containing 500 mg of potassium bromide, triturate to a homogeneous blend, dry in a vacuum desiccator at 60° for 3 h, and prepare a suitable disk.

Acceptance criteria: The IR absorption spectrum of the *Sample* exhibits maxima only at the same wavenumbers as that of the *Standard*.

ASSAY

- **Procedure**

Solution A: Dissolve 1.7 g of tetrabutylammonium hydrogen sulfate and 1.74 g of dibasic potassium phosphate in 1000 mL of water. Adjust with 1 N sodium hydroxide or phosphoric acid to a pH of 5.0.

Mobile phase: Methanol and *Solution A* (15:85)

System suitability solution: 0.4 mg/mL each of USP Hydroxyurea RS and hydroxylamine hydrochloride in *Mobile phase*

Standard solution: 0.4 mg/mL of USP Hydroxyurea RS in *Mobile phase*

Sample solution: Nominally 0.4 mg/mL of hydroxyurea in *Mobile phase* prepared as follows. Remove, as completely as possible, the contents of NLT 20 Capsules and grind to a fine powder. Transfer a portion of the powder, equivalent to 200 mg of hydroxyurea, to a 500-mL volumetric flask. Add 300 mL of *Mobile phase*, sonicate for 10 min, stir with the aid of a magnetic stirrer for 30 min, sonicate for an additional 10 min, and dilute with *Mobile phase* to volume. Filter a portion of the resulting solution, discarding the first 2 mL of the filtrate.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 0.5 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between hydroxylamine and hydroxyurea, *System suitability solution*

Column efficiency: NLT 5000 for hydroxyurea, *System suitability solution*

Tailing factor: NMT 1.5 for hydroxyurea, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydroxyurea ($CH_4N_2O_2$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of hydroxyurea from the *Sample solution*

r_S = peak response of hydroxyurea from the *Standard solution*

C_S = concentration of USP Hydroxyurea RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of hydroxyurea in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

▲**Test 1**▲ (TBD)

Medium: Water; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Analysis: Calculate the percentage of the labeled amount of hydroxyurea ($CH_4N_2O_2$) dissolved by using the procedure set forth in the *Assay*, making any necessary modifications.

Tolerances: NLT 80% (Q) of the labeled amount of hydroxyurea ($CH_4N_2O_2$) 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; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: Dissolve 1.7 g of tetrabutylammonium hydrogen sulfate and 1.74 g of dibasic potassium phosphate in 1000 mL of water. Adjust with phosphoric acid to a pH of 5.0.

Mobile phase: Methanol and *Buffer* (15:85)

Standard solution: (*L*/500) mg/mL of USP Hydroxyurea RS in *Medium*, where *L* is the label claim in mg/Capsule

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

Run time: NLT 4.5 times the retention time of hydroxyurea

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 hydroxyurea ($CH_4N_2O_2$) dissolved:

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

r_U = peak response of hydroxyurea from the *Sample solution*

r_S = peak response of hydroxyurea from the *Standard solution*

C_S = concentration of USP Hydroxyurea RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of hydroxyurea ($CH_4N_2O_2$) is dissolved. ▲ (TBD)

- **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, in a dry atmosphere.

Add the following:

▲- **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used. ▲ (TBD)

- **USP Reference Standards** ⟨11⟩

  USP Hydroxyurea RS

Page Information:

Not Applicable

Current DocID: