Hydroxyurea Capsules

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Expert Committee	Small Molecules 3

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 3 Expert Committee has revised the Hydroxyurea Capsules monograph. The purpose of this 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. 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*" has been updated to "*wavenumbers*", as it is the preferred terminology for infrared spectroscopy comparisons.

• *Dissolution Test 2* was validated using the Inertsil ODS-3 brand of column with L1 packing. The typical retention time for hydroxyurea is about 5 min.

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

The Hydroxyurea Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Yanyin Yang, Senior Scientist II (301-692-3623 or yanyin.yang@usp.org).

Revision Bulletin
Official: March 27, 2024

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▲ (RB 27-Mar-2024)

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. ▲ (RB 27-Mar-2024)

- **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. ▲ (RB 27-Mar-2024)

- **USP Reference Standards** ⟨11⟩

  USP Hydroxyurea RS

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