Aminocaproic Acid Tablets

Type of Posting	Revision Bulletin
Posting Date	10–Dec–2019
Official Date	11–Dec–2019
Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Aminocaproic Acid Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA approved drug products with different dissolution conditions and tolerance than the existing dissolution test. A *Labeling* section has also been added.

- *Dissolution Test 2* was validated using an GL Sciences Inertsil ODS-3V brand of L1 column. The typical retention time for aminocaproic acid is about 4 min.

The Aminocaproic Acid Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Edith Chang, Senior Scientific Liaison–Team Leader (301-816-8392 or yec@usp.org).

Aminocaproic Acid Tablets

DEFINITION

Aminocaproic Acid Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$).

IDENTIFICATION

• **A. Infrared Absorption** ⟨197K⟩

Sample: Triturate 2 Tablets with 10 mL of water, and filter into 100 mL of acetone. Swirl the mixture, and allow to stand for 15 min to complete crystallization. Pass the solution through a sintered-glass filter of medium pore size, and wash the crystals with 25 mL of acetone. Apply vacuum to remove the solvent, dry at 105° for 30 min, and cool. Use the residue.

Acceptance criteria: Meet the requirements

ASSAY

• **Procedure**

Sample solution: Nominally equivalent to about 500 mg of aminocaproic acid from NLT 20 finely powdered Tablets taken in a beaker in about 100 mL of glacial acetic acid. Heat gently to effect solution, and cool.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N perchloric acid in dioxane VS

Endpoint detection: Visual

Analysis: To the *Sample solution* add 10 drops of a 1-in-500 solution of crystal violet in chlorobenzene. Titrate with *Titrant* to a blue endpoint, and perform a blank determination. Each mL of 0.1 N perchloric acid is equivalent to 13.12 mg of aminocaproic acid ($C_6H_{13}NO_2$).

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 11-Dec-2019)

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer: Dissolve 6.185 g of boric acid and 7.930 g of potassium chloride in about 1000 mL of water, and add 60 mL of 1.0 N sodium hydroxide. Dilute with water to 2000 mL, and adjust if necessary with 1.0 N sodium hydroxide to a pH of 9.5 ± 0.1.

Standard solution: 0.5 mg/mL of USP Aminocaproic Acid RS in water

Sample solution: Filter a portion of the solution under test.

Blank: Water

Analysis: Into three separate 50-mL volumetric flasks pipet 1 mL each of *Sample solution*, *Standard solution*, and *Blank*. Add 20.0 mL of *Buffer* and 3.0 mL of a freshly prepared 1-in-500 solution of β-naphthoquinone-4-sodium sulfonate to each flask. Swirl to mix, and place the three flasks in a water bath maintained at a temperature of 65 ± 5° for 45 min. Cool, and dilute the contents of each flask with water to volume.

Determine the percentage of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$) dissolved from absorbances, at the wavelength of maximum absorbance at about 460 nm, from the *Sample solution* in comparison with those from the *Standard solution*, using the *Blank* to set the instrument.

Tolerances: NLT 75% (*Q*) of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$) 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 1: 100 rpm

Time: 30 min

Buffer A: Dissolve 500 mg of sodium 1-heptanesulfonate in 1 L of water. Add 1.0 mL of triethylamine and mix well.

Buffer B: Dissolve 13.3 g of monobasic sodium phosphate in 1 L of *Buffer A*, and mix well. Adjust with phosphoric acid to a pH of 2.20 ± 0.05.

[Note—The pH of *Buffer B* is critical because the diluent peak can coelute with the main peak even when the pH of *Buffer B* is at 2.10 or 2.30.]

Mobile phase: Methanol and *Buffer B* (25:75)

Standard solution: 1 mg/mL of USP Aminocaproic Acid RS in *Medium*. Sonication may be needed to aid the dissolution.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Temperatures

Autosampler: 25°

Column: 50°

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 2.5 times the retention time of aminocaproic acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$) dissolved:

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

r_U = peak response of aminocaproic acid from the *Sample solution*

r_S = peak response of aminocaproic acid from the *Standard solution*

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$) is dissolved.▲ (RB 11-Dec-2019)

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight 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 11-Dec-2019)

• **USP Reference Standards** ⟨11⟩

USP Aminocaproic Acid RS