Aminocaproic Acid Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	31–May–2019
Targeted Official Date	To Be Determined, Revision Bulletin
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 Aminocaproic Acid Tablets monograph.

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

- The analytical procedure in *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.

A *Labeling* section has been incorporated to support the inclusion of *Dissolution Test 2*.

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 Edith Chang, Senior Scientific Liaison–Team Leader (301-816-8392 or yec@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.

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**▲ (TBD)

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.▲ (TBD)

• **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.▲ (TBD)

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Aminocaproic Acid RS