Aminocaproic Acid Tablets

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<td>To Be Determined, Revision Bulletin</td>
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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 3. The Notice of Intent to Revise regarding Dissolution Test 2 is previously posted.

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

Labeling information has been incorporated to support the inclusion of Dissolution Test 3.

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 to the Chemical Medicines Monographs 2 Expert Committee (301-816-8392 or yec@usp.org).

¹This 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 (C₉H₁₄NO₃).

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
  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 (C₉H₁₄NO₃).
  Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• DISSOLUTION (711)
  Test 1A (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 (C₉H₁₄NO₃) 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 (C₉H₁₄NO₃) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 3.
  Medium: Water, degassed; 500 mL
  Apparatus 1: 100 rpm
  Time: 15 min
  Solution A: 0.55 g/L of sodium 1-heptanesulfonate in water
  Mobile phase: Transfer 10 g of monobasic potassium phosphate into a 1-L volumetric flask and dissolve with 300 mL of Solution A. Add 250 mL of methanol followed by another 300 mL of Solution A. Adjust with phosphoric acid to a pH of 2.2. Dilute with Solution A to volume.
  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 45-µm pore size.
  Chromatographic system
  (See Chromatography (621), System Suitability.)
  Mode: LC
  Detector: UV 210 nm
  Column: 4.6 mm × 15 cm; 5-µm packing
  Column temperature: 30°
  Flow rate: 0.7 mL/min
  Injection volume: 20 µL
  Run time: NLT 3.7 times the retention time of aminocaproic acid
  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 aminocaproic acid (C₉H₁₄NO₃) dissolved:
  Result = \(\frac{r_d}{r_t} \times C_d \times V \times (1/L) \times 100\)

  \(r_d\) = peak response of aminocaproic acid from the Sample solution
  \(r_t\) = peak response of aminocaproic acid from the Standard solution
  \(C_d\) = concentration of aminocaproic acid 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 (C₉H₁₄NO₃) is dissolved.

• 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.

• USP REFERENCE STANDARDS (11)
  USP Aminocaproic Acid RS