Aminocaproic Acid Tablets

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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 (C₆H₁₁NO₄).

**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°C 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 (C₆H₁₁NO₄).
  - **Acceptance criteria:** 95.0%–105.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution** (711)
  - **Test 1**
    - **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-sulfonate to each flask. Swirl to mix, and place the three flasks in a water bath maintained at a temperature of 65 ± 5°C 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 (C₆H₁₁NO₄) 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 (C₆H₁₁NO₄) 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°C
      - **Column:** 50°C
    - **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 (C₆H₁₁NO₄) dissolved:
      \[
      \text{Result} = \left(\frac{r_c}{r_s}\right) \times C \times V \times (1/L) \times 100
      \]
      \[
      r_c = \text{peak response of aminocaproic acid from the Sample solution}
      \]
      \[
      r_s = \text{peak response of aminocaproic acid from the Standard solution}
      \]
      \[
      C = \text{concentration of USP Aminocaproic Acid RS in the Standard solution (mg/mL)}
      \]
      \[
      V = \text{volume of Medium, 500 mL}
      \]
      \[
      L = \text{label claim (mg/Tablet)}
      \]
  - **Tolerances:** NLT 80% (Q) of the labeled amount of aminocaproic acid (C₆H₁₁NO₄) 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

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