Aminocaproic Acid Oral Solution

Type of Posting	Notice of Intent to Revise
Posting Date	31–Jan–2020
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, the Chemical Medicines Monographs 2 Expert Committee intends to revise the Aminocaproic Acid Oral Solution monograph as follows:

- Add *Identification B* based on the retention time agreement from the proposed *Assay*.
- Replace the titration procedure in the *Assay* with a liquid chromatographic procedure. The liquid chromatographic procedure was validated using the Inertsil ODS-3V brand of column with L1 packing from GL Sciences. The typical retention time for aminocaproic acid is about 5 min.
- Revise the *Acceptance criteria* in the *Assay* from 95.0%–115.0% to 90.0%–115.0% to accommodate the sponsor's specification. The *Definition* is revised accordingly.
- Add the requirements for *Deliverable Volume* <*698*>, and *Microbial Enumeration Tests* <*61*> and *Tests for Specified Microorganisms* <*62*>.
- Revise the storage condition based on the package insert from the approved manufacturer.

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).

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[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 Oral Solution

Change to read:

DEFINITION

Aminocaproic Acid Oral Solution contains NLT ▲90.0%▲ (TBD) and NMT 115.0% of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$).

IDENTIFICATION

Change to read:

• **A. ▲SPECTROSCOPIC IDENTIFICATION TESTS** ⟨197⟩**,** *Infrared Spectroscopy***:** 197K▲ (CN 1-May-2020)

Sample: Mix 1 g of ion-exchange resin (strongly acidic styrene–divinylbenzene cation-exchange resin) with 10 mL of 1 N hydrochloric acid in a 100-mL beaker. Decant and discard the hydrochloric acid, and wash the resin with five 10-mL portions of water, decanting and discarding the liquid following each washing. Place the washed resin in a 125-mL glass-stoppered, conical flask, and add a volume of Oral Solution, nominally equivalent to 250 mg of aminocaproic acid, and 10 mL of water. Insert the stopper in the flask, and shake by mechanical means for 30 min. Transfer the resin slurry to a sintered-glass funnel of medium pore size. Wash with 100 mL of water, filter by applying suction, and discard the washing. Place a beaker under the stem of the funnel, add 10 mL of 1 N hydrochloric acid to the resin, stir for 4–5 min, and filter by applying suction. Evaporate the filtrate on a steam bath to dryness, dry at 105° for 1 h, and cool.

Acceptance criteria: The residue meets the requirements.

Add the following:

▲• **B.** The retention time of the aminocaproic acid peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (TBD)

ASSAY

Change to read:

• **PROCEDURE**

▲Solution A: 10 g/L of potassium phosphate, monobasic and 0.55 g/L of sodium 1-heptanesulfonate in water. Adjust with sodium hydroxide to a pH of 6.8.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
20	50	50
25	100	0
35	100	0

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

Sample solution: Nominally 0.5 mg/mL of aminocaproic acid from Oral Solution in water

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 40°

Flow rate: 0.7 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of aminocaproic acid ($C_6H_{13}NO_2$) in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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)

C_U = nominal concentration of aminocaproic acid in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–115.0%▲ (TBD)

PERFORMANCE TESTS

Add the following:

▲• **DELIVERABLE VOLUME** ⟨698⟩**:** Meets the requirements▲ (TBD)

SPECIFIC TESTS

• **PH** ⟨791⟩**:** 6.0–6.5

Add the following:

▲• **MICROBIAL ENUMERATION TESTS** ⟨61⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** The total aerobic microbial count does not exceed 10^2 cfu/mL. The total yeasts and molds count does not exceed 10^1 cfu/mL. It meets the requirements of the tests for the absence of *Escherichia coli*.▲ (TBD)

ADDITIONAL REQUIREMENTS

Change to read:

• **PACKAGING AND STORAGE:** Preserve in tight containers.

▲Store at controlled room temperature.▲ (TBD)

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Aminocaproic Acid RS