Tranexamic Acid Tablets

Type of Posting	Revision Bulletin
Posting Date	26–Jul–2019
Official Date	01–Aug–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 Tranexamic 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/or tolerances than the existing dissolution test. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

- *Dissolution Test 2* was validated using the Zorbax 300-SCX brand of L9 column. The typical retention time for tranexamic acid is about 1.3 min.

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

Should you have any questions, please contact Wei Yang, Scientific Liaison (301-816-8338 or wiy@usp.org).

Add the following:

▲Tranexamic Acid Tablets

DEFINITION

Tranexamic Acid Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of tranexamic acid ($C_8H_{15}NO_2$).

IDENTIFICATION

• **A. INFRARED ABSORPTION** ⟨197K⟩

Sample: Finely powder 1 Tablet. Transfer a portion of the powdered Tablet, equivalent to 75 mg of tranexamic acid, to a suitable vial. Add 1 mL of water, mix on a vortex mixer for a few seconds, and sonicate for 1 min. Pass the suspension through a suitable filter onto a suitable watchglass. Evaporate the filtrate in an oven at 60° for 2 h, and then stir gently with a glass rod. Dry in an oven at 60° for another 1 h.

Acceptance criteria: The IR spectrum of the *Sample* corresponds to that of USP Tranexamic Acid RS.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **PROCEDURE**

Solution A: Dissolve 10.5 g of monobasic sodium phosphate monohydrate in 1000 mL of water, and add 8 mL of triethylamine followed by 2.3 g of sodium dodecyl sulfate. Adjust with 85% phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile and *Solution A* (15:85)

Standard solution: 2.6 mg/mL of USP Tranexamic Acid RS in water. Sonicate, if needed.

Sample solution: Nominally 2.6 mg/mL of tranexamic acid prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20), equivalent to 650 mg of tranexamic acid, to a 250-mL volumetric flask. Add about 200 mL of water, sonicate for about 20 min with occasional shaking, and dilute with water to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of tranexamic acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tranexamic acid ($C_8H_{15}NO_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

▲Test 1▲ (RB 1-Aug-2019)

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Solution A and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: Acetonitrile and *Solution A* (20:80)

Standard solution: 0.72 mg/mL of USP Tranexamic Acid RS in water. Sonicate, if needed. Pass the solution through a suitable filter of 0.45-µm pore size.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tranexamic acid ($C_8H_{15}NO_2$) dissolved:

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

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

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

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

V = volume of the *Medium*, 900 mL

L = label claim of tranexamic acid (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of tranexamic acid ($C_8H_{15}NO_2$) is dissolved.

▲Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: Simulated gastric fluid TS (without enzyme); 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 90 min

Buffer: Dissolve 45 g of monobasic potassium phosphate in 4.5 L of water. Adjust with phosphoric acid to a pH of 2.2.

Mobile phase: Acetonitrile and *Buffer* (10:90)

Standard solution: 0.72 mg/mL of USP Tranexamic Acid RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 5-cm; 5-µm packing L9

Column temperature: 25°

Flow rate: 1.2 mL/min

Injection volume: 15 µL

Run time: NLT 1.6 times the retention time of tranexamic acid

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 tranexamic acid ($C_8H_{15}NO_2$) dissolved:

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

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

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

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

V = volume of the *Medium*, 900 mL

L = label claim of tranexamic acid (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of tranexamic acid ($C_8H_{15}NO_2$) is dissolved. ▲ (RB 1-Aug-2019)

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

IMPURITIES

• **Organic Impurities**

Solution A and **Mobile phase:** Prepare as directed in the *Assay*.

System suitability solution: 20 µg/mL of USP Tranexamic Acid RS and 2 µg/mL of USP Tranexamic Acid Related Compound C RS in *Mobile phase*

Standard solution: 0.01 mg/mL of USP Tranexamic Acid RS in *Mobile phase*

Sample solution: Nominally 10 mg/mL of tranexamic acid in *Mobile phase* prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20), equivalent to 500 mg of tranexamic acid, to a 50-mL volumetric flask. Add about 40 mL of *Mobile phase*, sonicate for about 20 min with occasional shaking, and dilute with *Mobile phase* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 5.3 times the retention time of tranexamic acid

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between tranexamic acid and tranexamic acid related compound C, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified and any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of each specified or any unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tranexamic acid	1.0	—
Tranexamic acid related compound C[a]	1.1	—
Tranexamic acid related compound D[a, b]	1.2	—
Tranexamic acid related compound B[c]	1.6	0.3
Tranexamic acid related compound A[d]	2.3	0.2
Any unspecified degradation product	—	0.10
Total degradation products	—	0.5

[a] Process impurity controlled in the drug substance. It is included for identification purposes only. It should not be reported for the drug product, and should not be included in the total degradation products.

[b] 4-(Aminomethyl)benzoic acid.

[c] *cis*-4-(Aminomethyl)cyclohexanecarboxylic acid.

[d] *trans,trans*-4,4′-[Iminobis(methylene)]dicyclohexanecarboxylic acid.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store in well-closed containers, at controlled room temperature.

Add the following:

▲• **Labeling:** When more than one *Dissolution Test* is given, the labeling states the test used only if *Test 1* is not used. ▲ (RB 1-Aug-2019)

• **USP Reference Standards** ⟨11⟩

USP Tranexamic Acid RS

USP Tranexamic Acid Related Compound C RS

(*R,S*)-4-(Aminomethyl)cyclohex-1-enecarboxylic acid.

$C_8H_{13}NO_2$ 155.19 ▲ USP 1-Aug-2019