**TRANEXAMIC ACID**

Acidum tranexamicum

C₉H₁₄NO₃  \[M\_157.2\]

**DEFINITION**

trans-4-(Aminomethyl)cyclohexanecarboxylic acid.

**Content:** 99.0 per cent to 101.0 per cent (dried substance).

**CHARACTERS**

**Appearance:** white or almost white, crystalline powder.

**Solubility:** freely soluble in water and in glacial acetic acid, practically insoluble in acetone and in ethanol (96 per cent).

**TESTS**

**pH (2.2.3):** 7.0 to 8.0.

Dissolve 2.5 g in carbon dioxide-free water R and dilute to 50 mL with the same solvent.

**Related substances.** Liquid chromatography (2.2.29).

**Test solution.** Dissolve 0.20 g of the substance to be examined in water R and dilute to 20.0 mL with the same solvent.

- **Reference solution (a).** Dilute 5.0 mL of the test solution to 100.0 mL with water R. Dilute 1.0 mL of this solution to 10.0 mL with water R.

- **Reference solution (b).** Dissolve 20 mg of tranexamic acid CRS (containing impurity C) in water R and dilute to 2 mL with the same solvent.

- **Reference solution (c).** Dissolve 12 mg of 4-aminomethylbenzoic acid R (impurity D) in water R and dilute to 100 mL with the same solvent. Dilute 1.0 mL of the solution to 50 mL with water R. Dilute 5 mL of this solution to 200 mL with water R.

**Column:**

- **size:** \( l = 0.25 \text{ m}, d = 4.6 \text{ mm}\) or \( l = 0.25 \text{ m}, d = 6.0 \text{ mm}\);
- **stationary phase:** octadecylsilyl silica gel for chromatography R (5 μm).

**Mobile phase:** dissolve 11.0 g of anhydrous sodium dihydrogen phosphate R in 500 mL of water R and add 5 mL of triethylamine R and 1.4 g of sodium laurilsulfate R. Adjust to pH 2.5 with dilute phosphoric acid R and dilute to 600 mL with water R. Add 400 mL of methanol R and mix.

**Flow rate:** 0.9 mL/min.

**Detection:** spectrophotometer at 220 nm.

**Injection:** 20 μL.

**Run time:** 3 times the retention time of tranexamic acid.

**Identification of impurities:** use the chromatogram supplied with tranexamic acid CRS and the chromatogram obtained with reference solution (b) to identify the peak due to impurity C; use the chromatogram obtained with reference solution (c) to identify the peak due to impurity D.

**Relative retention** with reference to tranexamic acid (retention time = about 13 min); impurity C = about 1.1; impurity D = about 1.3; impurity B = about 1.5; impurity A = about 2.1.

**System suitability:** reference solution (b):

- **resolution:** minimum 1.5 between the peaks due to tranexamic acid and impurity C.

**Limits:**

- **correction factors:** for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 1.2; impurity C = 0.005; impurity D = 0.006;

- **impurity A:** not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

- **impurity B:** not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

- **unspecified impurities:** for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

- **sum of unspecified impurities:** not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

- **disregard limit:** 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.025 per cent).

**IDENTIFICATION**

Infrared absorption spectrophotometry (2.2.24).

**Preparation:** discs.

**Comparison:** tranexamic acid CRS.
Halides expressed as chlorides (2.4.4): maximum 140 ppm.
Dissolve 1.2 g in water R and dilute to 50 mL with the same solvent.

Heavy metals (2.4.8): maximum 10 ppm.
Dissolve 2.0 g in water R and dilute to 20 mL with the same solvent. 12 mL of this solution complies with test A. Prepare the reference solution using lead standard solution (1 ppm Pb) R.

Loss on drying (2.2.32): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulfated ash (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

ASSAY
Dissolve 0.140 g in 20 mL of anhydrous acetic acid R. Titrate with 0.1 M perchloric acid, determining the end-point potentiometrically (2.2.20).

1 mL of 0.1 M perchloric acid is equivalent to 15.72 mg of C₈H₁₅NO₂.

IMPURITIES
Specified impurities: A, B.
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use): C, D.

A. trans,trans-4,4′-iminodimethylene)di(cyclohexanecarboxylic) acid,

B. cis-4-(aminomethyl)cyclohexanecarboxylic acid,

C. (RS)-4-(aminomethyl)cyclohex-1-enecarboxylic acid,

D. 4-aminomethylbenzoic acid.