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Tranexamic Acid Tablets

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 2
Contact Details	helen.corns@mhra.gov.uk hannah.bowden@mhra.gov.uk
Deadline for Comment	30 September 2020
Target Publication Date (subject to change)	BP 2022
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Assay** New method - harmonised with new related substances test

Action and use

Antifibrinolytic.

DEFINITION

Tranexamic Acid Tablets contain Tranexamic Acid.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of tranexamic acid, $C_8H_{15}NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.5 g of Tranexamic Acid with 5 mL of *water* for 15 minutes, filter and add 2 mL of *ether* to the filtrate. Stir, add 10 mL of *methanol*, stir again and allow to crystallise. The crystals, after drying, comply with the following tests.

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of tranexamic acid (*RS 344*).

B. To 1 mL of a 1% w/v solution add 1 mL of a 0.2% w/v solution of *ninhydrin* in *ethanol* (*96%*) and heat on a water bath for 2 minutes. A dark bluish violet colour is produced.

C. Dissolve 0.2 g in 10 mL of 5M *sodium hydroxide*, add 0.2 mL of *benzoyl chloride* and shake vigorously for 10 minutes. Acidify to pH 4 with 2M *hydrochloric acid*, filter, wash the residue with 5 mL of *ether* and dry at 50° at a pressure of 2 kPa. The *melting point* of the residue is about 186°, Appendix V A.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in *water*.

(1) Shake a quantity of the powdered tablets containing 1 g of Tranexamic Acid with 100 mL for 10 minutes, filter and use the filtrate.
(2) 0.01% w/v of *tranexamic acid EPCRS*.
(3) 0.001% w/v of *4-aminomethylbenzoic acid*.
(4) 1% w/v of *tranexamic acid impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a Stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.9 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
Inject solution (1) and allow the chromatography to proceed for 3 times the retention time of tranexamic acid (about 13 minutes). Identify the impurities from the chromatogram obtained with solution (4) and from the reference chromatogram supplied with *tranexamic acid impurity standard BPCRS*.

MOBILE PHASE

Dissolve 11.0 g of *anhydrous sodium dihydrogen orthophosphate* in 500 mL of *water*, add 5 mL of *triethylamine* and 1.4 g of *sodium dodecyl sulfate*, adjust the pH to 2.5 with 2M *orthophosphoric acid* and add sufficient *water* to produce 600 mL. Add 400 mL of *methanol* and mix.

SYSTEM SUITABILITY

The test is not valid unless:

the chromatogram obtained with solution (4) closely resembles the reference chromatogram supplied with *tranexamic acid impurity standard BPCRS;*

the *resolution factor* between the peaks corresponding to tranexamic acid and impurity C in the chromatogram obtained with solution (4) is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any peak corresponding to impurity B is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%);

the area of any peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%);

the area of any other *secondary peak* is not greater than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in *water*.

(1) Shake a quantity of the powdered tablets containing 0.2 g of Tranexamic Acid with 100 mL for 10 minutes, filter and use the filtrate.
(2) 0.2% w/v of *tranexamic acid EPCRS*.

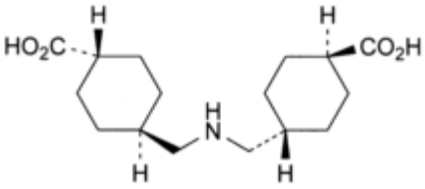
CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions under Related substances may be used.

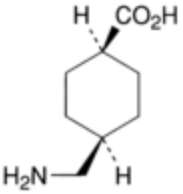
DETERMINATION OF CONTENT

Calculate the content of tranexamic acid, $C_8H_{15}NO_2$, in the tablets from the chromatograms obtained and using the declared content of $C_8H_{15}NO_2$, in *tranexamic acid EPCRS*.

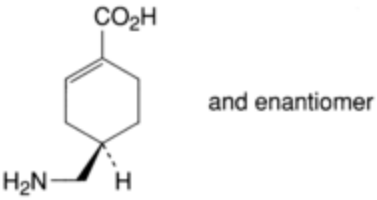
IMPURITIES



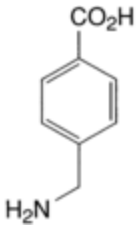
A. *trans,trans*-4,4′-(iminodimethylene)di(cyclohexanecarboxylic) acid,



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



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



D. 4-aminomethylbenzoic acid.