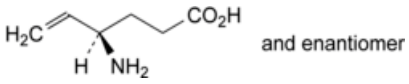
Edition: BP 2025 (Ph. Eur. 11.6 update)

Vigabatrin

General Notices

(Ph. Eur. monograph 2305)



and enantiomer

$C_6H_{11}NO_2$ 129.2 *60643-86-9*

Action and use

Antiepileptic.

Preparations

Vigabatrin Oral Powder

Vigabatrin Tablets

Ph Eur

DEFINITION

(4*RS*)-4-Aminohex-5-enoic acid.

Content

98.5 per cent to 101.5 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white powder.

Solubility

Freely soluble in water, slightly soluble in methanol, practically insoluble in methylene chloride.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison *vigabatrin CRS*.

TESTS

Related substances

Liquid chromatography (*2.2.29*).

Test solution Dissolve 50.0 mg of the substance to be examined in *water R*, using sonication if necessary, and dilute to 5.0 mL with the same solvent.

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

Reference solution (b) Dissolve 7.5 mg of *vigabatrin impurity A CRS* and 7.5 mg of *vigabatrin impurity B CRS* in *water R* and dilute to 50.0 mL with the same solvent. Dilute 2.0 mL of the solution to 20.0 mL with *water R*.

Reference solution (c) Dissolve 5.0 mg of *vigabatrin impurity E CRS* and 10.0 mg of *vigabatrin impurity D CRS* in *water R* and dilute to 50.0 mL with the same solvent. To 2.0 mL of the solution add 1.0 mL of reference solution (a) and dilute to 20.0 mL with *water R*.

Reference solution (d) Dilute 2 mL of reference solution (b) to 10 mL with *water R*.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped solid core phenylhexylsilyl silica gel for chromatography R* (2.7 µm);

— *temperature*: 45 °C.

Mobile phase Dissolve 2.1 g of *perfluoroheptanoic acid R* in a mixture of 195 mL of *methanol R2* and 805 mL of *water for chromatography R*.

Flow rate 1.0 mL/min.

Post-column solution *methanol R2*.

Post-column flow rate 0.8 mL/min.

Detection Charged aerosol detector (gas source: nitrogen at 35 psi) and, for impurities A and B, spectrophotometer at 210 nm.

Autosampler Set at 15 °C.

Injection 30 µL of the test solution and reference solutions (b), (c) and (d).

Run time 3 times the retention time of vigabatrin.

Identification of impurities Use the chromatogram obtained with the spectrophotometer and with reference solution (b) to identify the peaks due to impurities A and B; use the chromatogram obtained with the charged aerosol detector and with reference solution (c) to identify the peaks due to impurities D and E.

Relative retention With reference to vigabatrin (retention time = about 11 min): impurity A = about 0.3; impurity E = about 0.5; impurity D = about 0.6; impurity B = about 2.3.

System suitability:

— *resolution*: minimum 1.5 between the peaks due to impurities E and D in the chromatogram obtained with reference solution (c);

— *signal-to-noise ratio*: minimum 15 for the peak due to vigabatrin in the chromatogram obtained with reference solution (c); minimum 10 for the peak due to impurity B in the chromatogram obtained with reference solution (d);

— *symmetry factor*: minimum 0.6 for the peaks due to impurity D and vigabatrin in the chromatogram obtained with reference solution (c); minimum 0.6 for the peaks due to impurities A and B in the chromatogram obtained with reference solution (b).

Calculation of percentage contents:

— for impurities A and B, use the concentration of each impurity in reference solution (b);

— for impurity D, use the concentration of impurity D in reference solution (c);

— for impurities other than A, B and D, use the concentration of vigabatrin in reference solution (c).

Limits:

— *impurity D*: maximum 0.2 per cent;

— *impurities A, B (spectrophotometer at 210 nm)*: for each impurity, maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.05 per cent;

— *total*: maximum 0.5 per cent;

— *reporting threshold*: 0.03 per cent.

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 0.300 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

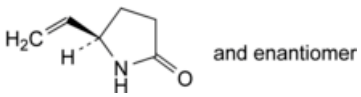
Dissolve 90 mg in 50 mL of *glacial acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 12.92 mg of $C_6H_{11}NO_2$.

IMPURITIES

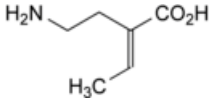
Specified impurities A, B, D.

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. 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) E.



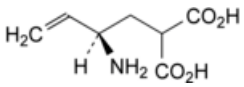
and enantiomer

A. (5*RS*)-5-ethenylpyrrolidin-2-one,



B. (2*E*)-2-(2-aminoethyl)but-2-enoic acid,

D. 4-aminobutanoic acid (GABA),



and enantiomer

E. 2-[(2*RS*)-2-aminobut-3-en-1-yl]propanedioic acid.

Ph Eur