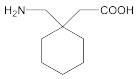
Gabapentin



$C_9H_{17}NO_2$ 171.24
Cyclohexaneacetic acid, 1-(aminomethyl)-.
1-(Aminomethyl)cyclohexaneacetic acid [60142-96-3].

» Gabapentin contains not less than 98.0 per cent and not more than 102.0 per cent of $C_9H_{17}NO_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers. Store at room temperature.

USP Reference standards ⟨11⟩**—**
USP Gabapentin RS
USP Gabapentin Related Compound A RS
2-Aza-spiro[4.5]decan-3-one.
$C_9H_{15}NO$ 153.22
USP Gabapentin Related Compound B RS
(1-Cyano-cyclohexyl)-acetic acid.
$C_9H_{13}NO_2$ 167.21
USP Gabapentin Related Compound D RS
(1-(3-Oxo-2-aza-spiro[4.5]dec-2-ylmethyl)-cyclohexyl)-acetic acid.
$C_{18}H_{29}NO_3$ 307.43
USP Gabapentin Related Compound E RS
Carboxymethyl-cyclohexanecarboxylic acid.
$C_9H_{14}O_4$ 186.21

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

pH ⟨791⟩**:** between 6.5 and 8.0, in a solution (1 in 50).

Water, *Method I* ⟨921⟩**:** not more than 0.5%.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩**:** 0.002%.

Related compounds—

LIMIT OF EARLY ELUTING IMPURITIES—

Diluent, Buffer solution, Mobile phase, and *Chromatographic system*—Proceed as directed in the *Assay*.

Impurities solution—Dissolve suitable quantities of USP Gabapentin Related Compound A RS and USP Gabapentin Related Compound B RS in methanol to obtain a solution containing about 1.4 mg per mL and 0.84 mg per mL, respectively.

System suitability solution—Dissolve a suitable quantity of USP Gabapentin RS in *Diluent,* and add an appropriate volume of *Impurities solution* to obtain a solution containing about 14.0 mg per mL, 0.014 mg per mL, and 0.0084 mg per mL of USP Gabapentin RS, USP Gabapentin Related Compound A RS, and USP Gabapentin Related Compound B RS, respectively.

Test solution—Use the *Assay preparation*.

Standard solution—Dissolve a suitable quantity of USP Gabapentin Related Compound E RS in *Diluent* to obtain a solution having a known concentration of 8.4 µg per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay*. Chromatograph the *System suitability solution* (about 20 µL), and record the peak responses as directed for *Procedure:* identify the major peaks using the relative retention times given in *Table 1:* the resolution, *R,* between gabapentin related compound A and gabapentin related compound B is not less than 2.3; and the relative standard deviation for gabapentin is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of any impurity in the portion of Gabapentin taken by the formula:

$$100(1/F)C_S / C_T)(r_i / r_S)$$

in which F is the relative response factor of the impurity (relative to gabapentin related compound E) according to *Table 1;* C_S is the concentration, in mg per mL, of USP Gabapentin Related Compound E RS in the *Standard solution;* C_T is the concentration of Gabapentin, in mg per mL, in the *Test solution;* r_i is the peak area for any impurity in the *Test solution;* and r_S is the peak area for gabapentin related compound E in the *Standard solution:* the impurities meet the requirements given in *Table 1*.

LIMIT OF LATE ELUTING IMPURITIES—

Diluent—Dissolve 2.32 g of ammonium phosphate monobasic in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.0.

Buffer solution—Proceed as directed in the *Assay*.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution,* acetonitrile, and methanol (35:35:30). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve an accurately weighed quantity of USP Gabapentin Related Compound D RS in a small amount of methanol, and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.0028 mg per mL.

Test solution—Use the *Assay preparation*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 215-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. The column temperature is maintained at 40°. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 13,600 theoretical plates for the gabapentin related compound D peak; and the relative standard deviation for replicate injections is not more than 7.0%.

Table 1

Compound Name	Relative Retention Time[1] (approximate)	Relative Response Factor[2]	Limit (%)
Gabapentin related compound E	2.9	1.0	0.10
Gabapentin related compound A	3.5	5.3	0.1
Gabapentin related compound B	3.8	0.35	0.06
Individual unknown impurity	—	0.41	0.10

[1] The relative retention times are calculated based on the retention time of gabapentin. [NOTE—This information is for identification purposes only.]

[2] The relative response factors are calculated based on the response of gabapentin related compound E due to the low absorptivity of gabapentin at the monitoring wavelength (215 nm).

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. [NOTE—Disregard all the peaks having relative retention times of 0.35 or less relative to gabapentin related compound D, as these are quantified in the test for *Limit of Early Eluting Impurities*.] Calculate the percentage of any impurity in the portion of Gabapentin taken by the formula:

$$100(1/F)(C_S / C_T)(r_i / r_S)$$

in which F is the relative response factor of the impurity (relative to gabapentin related compound D) which is 1.0 for gabapentin related compound D and 0.025 for all other impurities, respectively; C_S is the concentration, in mg per mL, of USP Gabapentin Related Compound D RS in the *Standard solution;* C_T is the concentration of Gabapentin, in mg per mL, in the *Test solution;* r_i is the peak area for any impurity in the *Test solution;* and r_S is the peak area for gabapentin related compound D in the *Standard solution:* not more than 0.10% of any impurity is found, and not more than 0.5% of total impurities (including the impurities quantified in *Limit of early eluting impurities*) is found.

Assay—

Diluent—Dissolve 2.32 g of monobasic ammonium phosphate in 1000 mL of water. Adjust with phosphoric acid to a pH of 2.0.

Buffer solution—Dissolve 0.58 g of monobasic ammonium phosphate and 1.83 g of sodium perchlorate in 1000 mL of water. Adjust with perchloric acid to a pH of 1.8.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (76:24). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability preparation—Quantitatively dilute a known volume of the *Standard preparation* with *Diluent* to obtain a solution having a concentration of about 2.3 mg per mL of gabapentin.

Standard preparation—Dissolve an accurately weighed quantity of USP Gabapentin RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 14.0 mg per mL.

Assay preparation—Transfer about 350 mg of Gabapentin, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 215-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. The column temperature is maintained at 40°. Chromatograph the *System suitability preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 1900 theoretical plates for the gabapentin peak. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0% for the gabapentin peak.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_9H_{17}NO_2$ in the portion of Gabapentin taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S and C_U are the concentrations of gabapentin, in mg per mL, in the *Standard preparation* and the *Assay preparation,* respectively; and r_U and r_S are the peak areas obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Gabapentin Capsules

» Gabapentin Capsules contain not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of gabapentin ($C_9H_{17}NO_2$).

Packaging and storage—Preserve in well-closed containers. Store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Gabapentin RS
USP Gabapentin Related Compound A RS
2-Aza-spiro[4.5]decan-3-one.
$C_9H_{15}NO$ 153.22

Identification—

A: *Infrared Absorption* ⟨197K⟩.

Test specimen—Empty the contents of not fewer than 10 Capsules, and grind to a fine powder. Use an amount of the powder, equivalent to 2 mg of gabapentin, and 200 mg of potassium bromide.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩**—**

Medium: 0.06 N hydrochloric acid (prepared by adding 51 mL of hydrochloric acid to 10 L of water); 900 mL.

Apparatus 2: 50 rpm.

Time: 20 minutes.

Determine the amount of gabapentin ($C_9H_{17}NO_2$) dissolved by employing the following method.

Mobile phase—Proceed as directed in the *Assay*.

Standard stock solution—Dissolve an accurately weighed quantity of USP Gabapentin RS in the *Medium* to obtain a solution having a known concentration of about 1.1 mg per mL.

Working standard solution—

FOR CAPSULES LABELED TO CONTAIN 100 MG—Transfer 10.0 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with *Medium* to volume.

FOR CAPSULES LABELED TO CONTAIN 300 MG—Transfer 30.0 mL of *Standard stock solution* to a 100-mL volumetric flask, and dilute with *Medium* to volume.

FOR CAPSULES LABELED TO CONTAIN 400 MG—Transfer 20.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, and dilute with *Medium* to volume.

Test solution—Pass a portion of the solution under test through a suitable 0.45-µm filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in the *Assay,* except to use the *Working standard solution*.

Procedure—Separately inject equal volumes (about 100 µL) of the appropriate *Working standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the amount of gabapentin ($C_9H_{17}NO_2$) dissolved by the formula:

$$\frac{r_U \times C_S \times 900 \times 100}{r_S \times L}$$

in which r_U and r_S are the peak responses for the *Working standard solution* and the *Test solution,* respectively; C_S is the concentration, in mg per mL, of the *Working standard solution*; 900 is the volume, in mL, of *Medium;* 100 is the conversion factor to percentage; and L is the Capsule label claim, in mg.

Tolerances—Not less than 80% *(Q)* of the labeled amount of gabapentin ($C_9H_{17}NO_2$) is dissolved in 20 minutes.