

## Gabapentin

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

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

### 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**— 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:

$$100(1/F)CS / CT)(r_i / r_S)$$

in which F is the relative response factor of the impurity (relative to gabapentin related compound E) according to [Table 1](#); CS is the concentration, in mg per mL, of [USP Gabapentin Related Compound E RS](#) in the Standard solution; CT is the concentration of Gabapentin, in mg per mL, in the Test solution; r<sub>i</sub> is the peak area for any impurity in the Test solution; and r<sub>S</sub> is the peak area for gabapentin related compound E in the Standard solution: the impurities meet the requirements given in [Table 1](#).

Table 1

Compound Name	Relative Retention Time <sup>1</sup> (approximate)	Relative Response Factor <sup>2</sup>	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

Compound Name	Relative Retention Time <sup>1</sup> (approximate)	Relative Response Factor <sup>2</sup>	Limit (%)
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).			

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**— 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%.

**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:

$$100(1/F)(CS / CT)(ri / rS)$$

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; CS is the concentration, in mg per mL, of [USP Gabapentin Related Compound D RS](#) in the Standard solution; CT is the concentration of Gabapentin, in mg per mL, in the Test solution; ri is the peak area for any impurity in the Test solution; and rS 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**— 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 °C. 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<sub>9</sub>H<sub>17</sub>NO<sub>2</sub> in the portion of Gabapentin taken by the formula:

$$100(CS / CU)(rU / rS)$$

in which CS and CU are the concentrations of gabapentin, in mg per mL, in the Standard preparation and the Assay preparation, respectively; and rU and rS are the peak areas obtained from the Assay preparation and the Standard preparation, respectively.