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 per centage of any impurity in the portion of Gabapentin taken by the formula:

\[
100\left(1/F\right)\left(C_i / C_0\right)\left(r_i / r_s\right)
\]

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; \( C_i \) is the concentration, in mg per mL, of USP Gabapentin Related Compound D RS in the Standard solution; \( C_0 \) is the concentration, 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 the 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°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 per centage of C9H17NO2 in the portion of Gabapentin taken by the formula:

\[
100\left(1/F\right)\left(C_i / C_0\right)\left(r_i / r_s\right)
\]

in which \( C_i \) and \( C_0 \) are the concentrations of gabapentin, in mg per mL, in the Standard preparation and the Assay preparation, respectively; and \( r_i \) 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 percent of the labeled amount of gabapentin (C9H17NO2).

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


Identification—

A: Infrared Absorption (179K).

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 (C9H17NO2) dissolved by employing the following method.

Chromatographic system (see Chromatography (621))—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 400 MG—Transfer 20.0 mL of the Standard stock solution to a 100-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 (C9H17NO2) dissolved by the formula:

\[
\frac{r_i \times C_i \times 900 \times 100}{r_s \times L}
\]

in which \( r_i \) and \( r_s \) are the peak responses for the Working standard solution and the Test solution, respectively; \( C_i \) 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 (C9H17NO2) is dissolved in 20 minutes.
Uniformity of dosage units (905): meet the requirements.

Related compounds—

Diluent—Prepare as directed in the Assay.

Solution A—Dissolve 1.2 g of monobasic potassium phosphate in 940 mL of water. Adjust with 5 N potassium hydroxide to a pH of 6.9, add 60 mL of acetonitrile, and stir. Filter, and degas.

Solution B—Dissolve 1.2 g of monobasic potassium phosphate in 700 mL of water. Adjust with 5 N potassium hydroxide to a pH of 6.9, add 300 mL of acetonitrile, and stir. Filter, and degas.

Mobile phase—Use variable mixtures of Solution A and Solution B as directed for Chromatographic system. Make adjustments if necessary (see System Suitability under Chromatography (621)).

Standard solution—Dissolve accurately weighed quantities of USP Gabapentin RS and USP Gabapentin Related Compound A RS in Diluent to obtain a solution having a known concentration of about 0.04 mg of each per mL.

Test solution—Remove and weigh the contents of not fewer than 20 Capsules. Transfer an accurately weighed portion of the powder, equivalent to about 500 mg of gabapentin, to a suitable volumetric flask, and dissolve the contents in Diluent with sonication, if necessary, for about 30 seconds. Dilute with Diluent to volume, and mix to obtain a final solution having a known concentration of about 20 mg per mL, based on the label claim.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 210-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
<th>Elution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0–4.0</td>
<td>100</td>
<td>0</td>
<td>isocratic</td>
</tr>
<tr>
<td>4.0–45.0</td>
<td>100–0</td>
<td>0–100</td>
<td>linear gradient</td>
</tr>
<tr>
<td>45.0–45.1</td>
<td>0–100</td>
<td>100–0</td>
<td>linear gradient</td>
</tr>
<tr>
<td>45.1–50.0</td>
<td>100</td>
<td>0</td>
<td>re-equilibration</td>
</tr>
</tbody>
</table>

Chromatograph the Standard solution, and record the peak responses as directed for Procedure: the tailing factor for the gabapentin peak is not more than 2.0; and the relative standard deviation for replicate injections for both gabapentin and gabapentin related compound A is not more than 5.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the responses for the gabapentin peak. Calculate the per centage of the labeled amount of gabapentin (C₉H₁₇NO₂) in the portion of Capsules taken by the formula:

\[ \frac{100(C_i / C_s)(r_0 / r_s)} \]

in which \( C_i \) is the concentration, in mg per mL, of USP Gabapentin Related Compound A RS in the Standard solution; \( C_s \) is the concentration, in mg per mL, of gabapentin in the Test solution; based on the label claim; and \( r_0 \) and \( r_s \) are the individual peak responses for gabapentin related compound A obtained from the Test solution and Standard solution, respectively; not more than 0.4% of gabapentin related compound A is found. Calculate the per centage of any other unspecified degradation product relative to gabapentin content in the portion of Capsules taken using the formula:

\[ \frac{100(C_i / C_s)(r_i / r_s)} \]

in which \( C_i \) is the concentration, in mg per mL, of USP Gabapentin RS in the Standard solution; \( C_s \) is the concentration, in mg per mL, of gabapentin in the Test solution, based on label claim; \( r_i \) is the response for each unspecified impurity in the Test solution; and \( r_s \) is the peak response for gabapentin in the Standard solution: not more than 0.1% of any individual unspecified impurity is found, and not more than 1.0% of total impurities is found.

ASSAY—

Diluent—Dissolve 1.2 g of monobasic potassium phosphate in 1 L of water. Adjust with 5 N potassium hydroxide to a pH of 6.9.

Mobile phase—Dissolve 1.2 g of monobasic potassium phosphate in 940 mL of water. Adjust with 5 N potassium hydroxide to a pH of 6.9, add 60 mL of acetonitrile, and stir. Filter, and degas. Make adjustments if necessary (see System Suitability under Chromatography (621)).

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 4.0 mg per mL.

Test solution—Remove and weigh the contents of not fewer than 20 Capsules. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of gabapentin, to a suitable volumetric flask, and dissolve the contents in Diluent with sonication, if necessary, for about 60 seconds. Dilute with Diluent to volume, and mix to obtain a final solution having a known concentration of about 4.0 mg per mL.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 210-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1.2 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the column efficiency is not less than 7,000 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the gabapentin peak. Calculate the per centage of the labeled amount of gabapentin (C₉H₁₇NO₂) in the portion of Capsules taken by the formula:

\[ \frac{100(C_i / C_s)(r_0 / r_s)} \]

in which \( C_i \) is the concentration, in mg per mL, of USP Gabapentin RS in the Standard preparation; \( C_s \) is the concentration, in mg per mL, of gabapentin in the Assay preparation, based on the label claim; and \( r_0 \) and \( r_s \) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Gabapentin Tablets

DEFINITION

Gabapentin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of gabapentin (C₉H₁₇NO₂).

IDENTIFICATION

A. INFRARED ABSORPTION (197K)

Sample: Grind at least 20 Tablets to a fine powder. Use an amount of powder equivalent to 2 mg of gabapentin and 200 mg of dry potassium bromide.

B. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY—

PROCEDURE

Diluent: 1.2 g/L of monobasic potassium phosphate in water. Adjust with 5 N potassium hydroxide to a pH of 6.9.

Mobile phase: Acetonitrile and Diluent (3:47)

Standard solution: 4.0 mg/mL of USP Gabapentin RS in Diluent

Sample solution: 4.0 mg/mL of gabapentin from NL T 20 finely powdered Tablets in Diluent