Test solution—Transfer about 250 mg of Ipratropium Bromide, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix.

Chromatographic system (see Chromatography (621))—Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the relative retention times are listed in the accompanying table; the resolution, \( R_n \), between ipratropium and ipratropium related compound B is not less than 4; the tailing factor of the ipratropium peak is not more than 2.5; and the relative standard deviation for replicate injections is not more than 5%.

Procedure—Separately inject equal volumes (about 5 \( \mu L \)) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of related compounds in the portion of Ipratropium Bromide taken by the formula:

\[
100(1/F)(C_r / C_t)(r_r / r_t)
\]

in which \( F \) is the relative response factor of the related compound relative to ipratropium bromide; \( C_t \) is the concentration, in mg per mL, of USP Ipratropium Bromide RS in the Standard solution; \( C_r \) is the concentration, in mg per mL, of Ipratropium Bromide in the Test solution; \( r_r \) is the individual peak response of the individual related compound; and \( r_t \) is the peak response of ipratropium in the Standard solution. See the accompanying table for relative retention times, relative response factors, and acceptance criteria.

<table>
<thead>
<tr>
<th>Related Compound</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Limit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium related compound ( C^1 )</td>
<td>0.7</td>
<td>3.8</td>
<td>0.10</td>
</tr>
<tr>
<td>Ipratropium bromide</td>
<td>1.0</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Ipratropium related compound B (8S,8R)-ipratropium bromide ( 2 )</td>
<td>1.3</td>
<td>1.0</td>
<td>0.10</td>
</tr>
<tr>
<td>N-isopropyl(oratropinium bromide ( 3 )</td>
<td>2.3</td>
<td>1.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Apo-ipratropium bromide ( 4 )</td>
<td>5.1</td>
<td>2.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Any individual unknown impurity</td>
<td>—</td>
<td>—</td>
<td>0.10</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>0.25</td>
</tr>
</tbody>
</table>

\( 1^{(2R,3)}-3\text{-Hydroxy-2-phenylpropanoic acid.} \)

\( 2^{(1R,3,5,5,8,8)}-3\text{-Hydroxy-2-phenylpropanoyl]oxy-8-methyl-8-(1-methylethyl) 8-azoniabicyclo[3.2.1]octane, bromide.} \)

\( 3^{(1R,3,5,5,8)-8-(1\text{-Methylthethyl}) 8-azabicyclo[3.2.1]oct-3-y(2R,3)-3\text{-Hydroxy-2-phenylpropanoate.} \)

\( 4^{(1R,3,5,5,8)-8-(1\text{-Methylthethyl}) 3\text{-[(2-phenylpropenoyl]oxy-8-azoniabicyclo[3.2.1]octane.} \)

Assay—

Phosphate solution—Transfer 8.9 g of dibasic sodium phosphate dihydrate to a 100-mL volumetric flask. Dissolve in and dilute with water to volume, and mix.

Buffer—Transfer 14.3 g of monobasic sodium phosphate dihydrate and 2.0 g of tetrapropylammonium chloride to a 1-L volumetric flask, dissolve in and dilute with water to volume, and mix. Adjust with Phosphate solution to a pH of 5.5 ± 0.2. Pass through a nylon membrane filter having a porosity of 0.45 \( \mu m \) or finer.

Mobile phase—Prepare a filtered and degassed mixture of Buffer and methanol (87:13). [NOTE—Do not use the Mobile phase after 36 hours.] Make adjustments if necessary (see System Suitability under Chromatography (621)).

System suitability solution—Dissolve suitable quantities of USP Ipratropium Bromide RS and USP Ipratropium Related Compound C RS in Mobile phase and dilute quantitatively, and stepwise if necessary, with Mobile phase to obtain a solution having a known concentration of about 0.5 mg per mL and 0.1 mg per mL, respectively.

Standard preparation—Dissolve an accurately weighed quantity of USP Ipratropium Bromide RS in Mobile phase, and dilute quantitatively, and stepwise if necessary, with Mobile phase to obtain a solution having a known concentration of about 0.5 mg per mL.

Assay preparation—Transfer about 50 mg of Ipratropium Bromide, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 220-nm detector and a 3.9-mm \( \times \) 15-cm column that contains 4- \( \mu m \) packing L1. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 30 °C. Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the relative retention times are about 0.7 for ipratropium related compound C and 1.0 for ipratropium bromide; the resolution, \( R_n \), between ipratropium related compound C and ipratropium is not less than 4; the tailing factor of the ipratropium peak is not more than 2.5; and the relative standard deviation for replicate injections is not more than 1.6%.

Procedure—Separately inject equal volumes (about 5 \( \mu L \)) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in percent, of \( C_{20} H_{30} Br NO_3 \cdot H_2 O \) in the portion of Ipratropium Bromide taken by the formula:

\[
100(C_t / C_r)(r_r / r_t)
\]

in which \( C_t \) is the concentration, in mg per mL, of USP Ipratropium Bromide RS in the Standard preparation; \( C_r \) is the concentration, in mg per mL, of Ipratropium Bromide in the Assay preparation; and \( r_r \) and \( r_t \) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Irbesartan

\[
C_{25} H_{30} N_6 O_2 \quad 428.53
\]

Ipratropium / Official Monographs

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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.

Water, Method I (921): not more than 0.5%.

Heavy metals, Method II (231): 0.002%

Limit of azide—

Mobile phase—Prepare a filtered and degassed 0.1 N sodium hydroxide solution (see System Suitability under Chromatography (621)).

Standard solution—Transfer about 25 mg of sodium azide, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix. Pipet 250 µL of this solution into a 200-mL volumetric flask, dilute with Mobile phase to volume, and mix. This solution contains about 0.312 µg of sodium azide per mL.

Test solution—Transfer about 100 mg of irbesartan, accurately weighed, to a 5-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a conductimetric detector [note—A suitable background suppression unit may be used.] and a 4.0-mm × 25-cm column that contains packing L31. The flow rate is about 1.0 mL per minute. Chromatograph the Standard solution, and record the peak responses as directed for Procedure: the signal-to-noise ratio for the azide peak is not less than 10.

Procedure—Separately inject equal volumes (about 200 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the peak areas for azide. Calculate the amount of azide, in ppm, in the portion of irbesartan taken by the formula:

\[
100(C_S / C_T)(42.02/65.01)(r_U / r_S)
\]

in which \( C_S \) is the concentration, in µg per mL, of sodium azide in the Standard solution; \( C_T \) is the concentration, in mg per mL, of irbesartan in the Test solution; \( r_U \) is the peak area for azide obtained from the Test solution; and \( r_S \) is the peak area for azide obtained from the Standard solution: not more than 10 ppm of azide is found.

Related compounds—

pH 3.2 Phosphate buffer and Mobile phase—Proceed as directed in the Assay.

Standard solution—Prepare as directed for the System Suitability solution in the Assay.

Test solution—Dissolve an accurately weighed quantity of irbesartan in methanol to obtain a solution having a known concentration of about 1 mg per mL.

Chromatographic system (see Chromatography (621))—Proceed as directed in the Assay. Chromatograph the Standard solution and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the area for the irbesartan related compound A peak. Calculate the per cent age of irbesartan related compound A in the portion of irbesartan taken by the formula:

\[
100(C_S / C_T)(r_U / r_S)
\]

in which \( C_S \) is the concentration, in mg per mL, of USP Irbesartan Related Compound A RS in the Standard solution; \( C_T \) is the concentration, in mg per mL, of Irbesartan in the Test solution; \( r_U \) is the peak response for irbesartan related compound A obtained from the Test solution; and \( r_S \) is the peak response for irbesartan related compound A obtained from the Standard solution.

Calculate the percentage of other impurities in the portion of irbesartan taken by the formula:

\[
100(C_S / C_T)(r_U / r_S)
\]

in which \( C_S \) is the concentration, in mg per mL, of USP Irbesartan RS in the Standard solution; \( C_T \) is the concentration, in mg per mL, of Irbesartan in the Test solution; and \( r_U \) and \( r_S \) are the peak responses for each of the other impurities and USP Irbesartan RS obtained from the Test solution and the Standard solution, respectively: not more than 0.2% of irbesartan related compound A is found; not more than 0.1% of any other impurity is found; and not more than 0.5% of total impurities is found.

Assay—

pH 3.2 Phosphate buffer—Mix 5.5 mL of phosphoric acid with about 950 mL of water, and adjust pH to 3.2 with triethylamine.

Mobile phase—Prepare a filtered and degassed mixture of pH 3.2 phosphate buffer and acetonitrile (67:33). Make adjustments if necessary (see System Suitability under Chromatography (621)).

System suitability solution—Dissolve accurately weighed quantities of USP Irbesartan RS and USP Irbesartan Related Compound A RS in methanol to obtain a solution having a known concentration of about 0.5 mg per mL of each USP Reference Standard.

Standard preparation—Dissolve an accurately weighed quantity of USP Irbesartan RS in methanol to obtain a solution having a known concentration of about 0.5 mg per mL.

Assay preparation—Transfer about 50 mg of irbesartan, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.0-mm × 25-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the Standard preparation, and record the peak response as directed for Procedure: the retention time of the major peak in the chromatogram is 1.0±0.2 min. The flow rate is about 1.0 mL per minute. Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 2.0.

Procedure—Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for all the peaks. Calculate the quantity, in mg, of C₂₅H₂₈N₆O in the portion of irbesartan taken by the formula:

\[
100(C_S / C_T)(r_U / r_S)
\]

in which \( C_S \) is the concentration, in mg per mL, of USP Irbesartan RS in the Standard preparation; and \( r_U \) and \( r_S \) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Irbesartan Tablets

Irbesartan Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of irbesartan (C₂₅H₂₈N₆O₃).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards (11)—

USP Irbesartan RS
USP Irbesartan Related Compound A RS