**Assay**—Into a 100-mL volumetric flask containing 2.5 mL of water and 1 mL of sodium hydroxide TS 2, introduce 1.0 g of the solution to be examined, shake, and dilute with water to 100.0 mL. To 10.0 mL of the solution add 30.0 mL of 0.1 N iodine VS. Mix, and add 10 mL of sodium hydroxide TS 2. After 15 minutes, add 25 mL of diluted sulfuric acid and 4 mL of starch TS. Titrate with 0.1 N sodium thiosulfate VS. Each 1 mL of 0.05 M iodine is equivalent to 1.501 mg of \( \text{CH}_2\text{O} \).

**Formoterol Fumarate**

\[(\text{C}_19\text{H}_{24}\text{N}_2\text{O}_4)_2 \cdot \text{C}_4\text{H}_4\text{O}_4 \cdot 2\text{H}_2\text{O} \quad 840.91\]

Test solution—

\[15 \text{ minutes, add } 25 \text{ mL of diluted sulfuric acid and } 4 \text{ mL of and } +0.10 \text{ iodine VS. Mix, and add } 10 \text{ mL of sodium hydroxide TS 2. After } \text{Optical rotation, } 100.0 \text{ mL. To } 10.0 \text{ mL of the solution add } 30.0 \text{ mL of } 0.1 \text{ N } \text{USP Formoterol Fumarate, and formoterol related compounds A, B, C, D, E, F, G, and H.} \]

**Assay**

Formoterol Fumarate contains not less than 98.5 percent and not more than 101.5 percent of \((\text{C}_19\text{H}_{24}\text{N}_2\text{O}_4)_2 \cdot \text{C}_4\text{H}_4\text{O}_4\), calculated on the anhydrous basis.

**Packaging and storage**—Preserve in well-closed, light-resistant containers.

**Labeling**—The labeling states with which **Content of related compound I** the test article complies if a test other than **Content of related compound I, Test I** is used.

**USP Reference standards** (11)—

USP Formoterol Fumarate RS

USP Formoterol Fumarate System Suitability Mixture RS

It is a mixture of USP Formoterol Fumarate RS and formoterol related compounds A, B, C, D, E, F, G, and H.


**Formoterol related compound G**: (2R)-1-(4-Methoxyphenyl)propan-2-amine.

**Formoterol related compound H**: N-[5-[[1R]-2-[Benzy[[1R]-2-[[2-(4-methoxyphenyl)-1-methylthethyl]amino]-1-hydroxyethyl]-2-hydroxyphenyl]formamide (mono-benzyl analogue).

**USP Formoterol Resolution Mixture RS**

This standard is a mixture of formoterol and formoterol fumarate impurity I.


**Identification**: Infrared Absorption (197K).

**Optical rotation**, Angular Rotation (781A): between –0.10° and +0.10°.

**Test solution**: 10 mg per mL, in methanol.

**pH** (791J): between 5.5 and 6.5, in a solution in water containing 1 mg per mL.

**Water, Method I** (921J): between 4.0% and 5.0%.

**Residue on ignition** (281): not more than 0.1%, determined on 1 g.

**Heavy metals**, Method II (231J): not more than 0.002%.

**Related compounds**—

Solution A—Dissolve 3.73 g of sodium dihydrogen phosphate monohydrate and 0.35 g of phosphoric acid in water, dilute with water to 1000 mL, and mix. The pH of this solution is 3.1 ± 0.1.

Solution B—Use acetonitrile.

**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 (621J)).

**Solution C**—Transfer 6.10 g of sodium dihydrogen phosphate monohydrate and 1.03 g of disodium hydrogen phosphate dihydrate to a 1000-mL volumetric flask, add 500 mL of water, and dissolve. Dilute with water to volume, and mix. The pH is 6.0 ± 0.1.

**Diluent**—Prepare a filtered and degassed mixture of Solution C and acetonitrile (84:16, v/v).

**System suitability solution**—Transfer about 5 mg of USP Formoterol Fumarate System Suitability Mixture RS (containing formoterol fumarate, and formoterol related compounds A, B, C, D, E, F, G, and H), accurately weighed, to a 25-mL volumetric flask, add 10 mL of Diluent, and sonicate to dissolve. Dilute with Diluent to volume, and mix.

**Test solution**—Transfer about 20.0 mg of Formoterol Fumarate, accurately weighed, to a 100-mL volumetric flask, add 50 mL of Diluent, and sonicate to dissolve. Dilute with Diluent to volume, and mix.

**Chromatographic system** (see Chromatography (621J))—The liquid chromatograph is equipped with a 214-nm detector and a 4.6-mm × 15-cm column that contains packing L7. The flow rate is about 1.0 mL per minute. The chromatogram 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</td>
<td>84</td>
<td>16</td>
<td>equilibration</td>
</tr>
<tr>
<td>0–10</td>
<td>84</td>
<td>16</td>
<td>isocratic</td>
</tr>
<tr>
<td>10–37</td>
<td>84–30</td>
<td>16→70</td>
<td>linear gradient</td>
</tr>
<tr>
<td>37–40</td>
<td>30→84</td>
<td>70→16</td>
<td>linear gradient</td>
</tr>
<tr>
<td>40–55</td>
<td>84</td>
<td>16</td>
<td>isocratic</td>
</tr>
</tbody>
</table>

Chromatograph the **System suitability solution**, and record the peak responses as directed for **Procedure**: the resolution, \( R_s \), between formoterol related compound G and formoterol related compound A is not less than 1.5; the peak-to-valley ratio (\( H_t \) / \( H_v \)) of formoterol related compound C and formoterol is not less than 2.5, where \( H_t \) is the height above the baseline of the peak due to formoterol related compound C, and \( H_v \) is the height above the baseline of the lowest point of the curve separating this peak from the peak due to formoterol; and the relative retention times and limits are as provided in **Table 1**.
Chromatographic Reagents

- Potassium phosphate solution
- Potassium phosphate, trihydrate, in 1000 mL of water, and mix.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 225-nm detector and a 4.6-mm × 15-cm column that contains packing L67 (see Chromatographic Reagents under Reagents, Indicators, and Solutions). The flow rate is about 0.5 mL per minute. Chromatograph the Standard solution, and record the peak responses as directed for the Procedure: the peak-to-valley ratio (Hv/Hs) of formoterol related compound I and formoterol is not less than 2.5, where Hv is the height above the baseline of the peak due to formoterol related compound I, and Hs is the height above the baseline of the lowest point of the curve separating this peak from the peak due to formoterol.

Procedure—Separately inject equal volumes (about 2 µL of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the peak responses for formoterol related compound I and formoterol. Disregard all other peaks. Calculate the percentage of formoterol related compound I in the portion of Formoterol Fumarate taken by the formula:

\[ 100\left(\frac{r_s}{r_F}\right) \]

in which \( r_F \) is the peak response for formoterol related compound I, and \( r_s \) is the sum of the responses of both formoterol and formoterol related compound I peaks: not more than 0.3% of formoterol related compound I is found.

TEST 2—

Potassium phosphate solution—Dissolve 5.3 g of tribasic potassium phosphate, trihydrate, in 1000 mL of water, and mix. Adjust the pH with potassium hydroxide or phosphoric acid to 12.0 ± 0.1.

Mobile phase—Prepare a filtered degassed mixture of Potassium phosphate solution and acetonitrile (88:12). Standard solution—Dissolve 5 mg of USP Formoterol Fumarate Reference Standard in 10 mL of the Mobile phase, dilute with water to 25 mL, and mix. Test solution—Dilute 5 mg of Formoterol Fumarate in water, dilute with water to 50 mL, and mix. Diluted test solution—Dilute 1 mL of the Test solution with water to 25 mL. Chromatograph the Diluted test solution: the chromatogram obtained with the Diluted test solution: not more than 0.3% of formoterol related compound I is found.

TEST 3—

Potassium dihydrogen phosphate solution—Dissolve 6.9 g of potassium dihydrogen phosphate and 12.0 g of disodium hydrogen phosphate in 1000 mL of water, and mix.

Mobile phase—Prepare a filtered degassed mixture of Water and acetonitrile (85:15). Standard solution—Dissolve 5 mg of USP Formoterol Fumarate Reference Standard in 10 mL of the Mobile phase, dilute with water to 25 mL, and mix. Test solution—Dilute 5 mg of Formoterol Fumarate in water, dilute with water to 50 mL, and mix. Chromatograph the Test solution: the chromatogram obtained with the Test solution: not more than 0.3% of formoterol related compound I is found.

Potassium dihydrogen phosphate solution—Dissolve 6.9 g of potassium dihydrogen phosphate and 12.0 g of disodium hydrogen phosphate in 1000 mL of water, and mix.

Mobile phase—Prepare a filtered degassed mixture of Water and acetonitrile (85:15). Standard solution—Dissolve 5 mg of USP Formoterol Fumarate Reference Standard in 10 mL of the Mobile phase, dilute with water to 25 mL, and mix. Test solution—Dilute 5 mg of Formoterol Fumarate in water, dilute with water to 50 mL, and mix. Chromatograph the Diluted test solution: the chromatogram obtained with the Diluted test solution: not more than 0.3% of formoterol related compound I is found.

Asy—Transfer about 350 mg of Formoterol Fumarate, accurately weighed, to a titration vessel, dissolve in 50 mL of anhydrous acetic acid, and titrate with 0.1 M perchloric acid VS, determining the end point potentiometrically. Per form a blank determination, and make any necessary correction. Each mL of 0.1 M perchloric acid is equivalent to 40.24 mg of \( \text{C}_{18}\text{H}_{21}\text{N}_{2}\text{O}_{7} \cdot \text{C}_{6}\text{H}_{6}\text{O}_{3}. \)

**Table 1**

<table>
<thead>
<tr>
<th>Related Compound</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor (f)</th>
<th>Limit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>0.4</td>
<td>2.64</td>
<td>0.1</td>
</tr>
<tr>
<td>A</td>
<td>0.5</td>
<td>1.75</td>
<td>0.3</td>
</tr>
<tr>
<td>B</td>
<td>0.7</td>
<td>1.00</td>
<td>0.2</td>
</tr>
<tr>
<td>C</td>
<td>1.2</td>
<td>1.10</td>
<td>0.2</td>
</tr>
<tr>
<td>D</td>
<td>1.3</td>
<td>1.12</td>
<td>0.2</td>
</tr>
<tr>
<td>E</td>
<td>1.8</td>
<td>0.67</td>
<td>0.1</td>
</tr>
<tr>
<td>F</td>
<td>2.0</td>
<td>1.00</td>
<td>0.2</td>
</tr>
<tr>
<td>H</td>
<td>2.2</td>
<td>1.24</td>
<td>0.1</td>
</tr>
<tr>
<td>Any other individual impurity</td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Total unspecified impurities</td>
<td></td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
</tbody>
</table>

* 2(RS)-1-(4-Methoxyphenyl)propan-2-amine.
* 1-(3-Amino-4-hydroxyphenyl)-2-[[2-(4-methoxyphenyl)-1-methylethyl]amino]ethanol.

![Image of Foscarnet Sodium](image-url)

**Foscarnet Sodium**

\( \text{CNa}_3\text{O}_8\text{P} \cdot 6\text{H}_2\text{O} \ 300.04 \)

Phosphinecarboxylic acid, dihydroxy-, oxide, trisodium salt, hexahydrate.

Phosphonoformic acid, trisodium salt, hexahydrate [34156-56-4].