Erythromycin Stearate Tablets

Erythromycin Stearate Tablets contain the equivalent of not less than 90.0 per cent and not more than 120.0 per cent of the labeled amount of erythromycin (C_{37}H_{67}NO_{13}).

Packaging and storage—Preserve in tight containers.

USP Reference standards (11)—
USP Erythromycin RS
USP Erythromycin Stearate RS

Identification—To a quantity of powdered tablets add a volume of methanol sufficient to yield a solution containing the equivalent of about 5 mg of erythromycin per mL. Shake this mixture by mechanical means for about 30 minutes. Centrifuge a portion of this mixture, and use the clear supernatant as the test solution. Prepare a Standard solution of USP Erythromycin Stearate RS in methanol containing about 8 mg per mL. Apply separately 20 µL each of the test solution and the Standard solution to a suitable thin-layer chromatographic plate (see Chromatography (621)) coated with a 0.25-mm layer of chromatographic silica gel mixture, and allow to dry. Place the plate in an unlined chromatographic chamber, and develop the chromatograms in a solvent system consisting of a mixture of methanol and chloroform (85:15) until the solvent front has moved about 9 cm. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray the plate with a methanolic solution of 2′,7′-dichlorofluorescein (1 in 500), and examine the plate under long-wavelength UV light: the Rf values of the principal fluorescent spots obtained from the test solution correspond to those obtained from the Standard solution. Then spray the plate with a mixture of dehydrated alcohol, p-methoxybenzaldehyde, and sulfuric acid (90:5:5). Heat the plate at 100 °C for 10 minutes, and examine the chromatograms, in which the erythromycin appears as a black-to-purple spot: the Rf value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Dissolution (711)—
Medium: 0.05 M pH 6.8 phosphate buffer (see under Solutions in the section Reagents, Indicators, and Solutions); 900 mL.
Apparatus 2: 120 minutes.

Stock standard solution—Dissolve an accurately weighed quantity of USP Erythromycin RS in methanol to obtain a solution containing about 14 mg per mL. Dilute quantitatively with water to 50.0 mL, and mix. A working solution of about 0.56 mg of USP Erythromycin RS per mL.
Working standard solution—On the day of use, dilute 25.0 mL of Stock standard solution with water to 50.0 mL, and mix.

Test solution—After 120 minutes, withdraw a portion of the solution under test, filter, and dilute with Medium, if necessary, to obtain a solution having an estimated concentration of about 0.28 mg of erythromycin per mL.

Procedure—Transfer 5.0-mL portions of the Working standard solution to 25-mL volumetric flasks, one of which serves as a working standard blank. Similarly, transfer 5.0-mL portions of the Test solution to 25-mL volumetric flasks, one of which serves as a blank for that Test solution. To each of the flasks designated as a blank add 2.0 mL of 0.5 N sulfuric acid and to the remaining flasks add 2.0 mL of water. Allow to stand for 5 minutes with intermittent swirling. To all flasks add 15.0 mL of 0.25 N sodium hydroxide, dilute with Medium to volume, and mix. Heat the flasks in a water bath at 60 ± 0.5 °C for 5 minutes, and allow to cool. Using a suitable spectrophotometer, determine the absorbance of each solution, corrected for its blank solution, at the wavelength of maximum absorbance at about 236 nm. Determine the amount of C_{37}H_{67}NO_{13} dissolved from the Test solution in comparison with the solution obtained from the Working standard solution.

Tolerances—Not less than 75% (Q) of the labeled amount of C_{37}H_{67}NO_{13} is dissolved in 120 minutes.

Uniformity of dosage units (905): meet the requirements.
Loss on drying (731)—Dry about 100 mg of powdered tablets in a capillary-stoppered bottle in vacuum at 60 °C for 3 hours: it loses not more than 5.0% of its weight.

Assay—Proceed with Tablets as directed in the Assay under Erythromycin Tablets.

Escitalopram Oxalate

C_{20}H_{21}FN_{2}O \cdot CS_{2}H_{2}O_{4} \quad 414.43
S-(+)-5-Isofenoxylarboxonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroxy-oxalate; in an unlined chromatographic chamber, and develop the chromatographic silica gel mixture, and allow to dry. Place the plate in an unlined chromatographic chamber, and develop the chromatograms obtained from the test solution and the Standard solution in a suitable thin-layer chromatographic plate.

Identification—To a quantity of powdered tablets add a volume of methanol sufficient to yield a solution containing the equivalent of about 5 mg of erythromycin per mL. Shake this mixture by mechanical means for about 30 minutes. Centrifuge a portion of this mixture, and use the clear supernatant as the test solution. Prepare a Standard solution of USP Erythromycin Stearate RS in methanol containing about 8 mg per mL. Apply separately 20 µL each of the test solution and the Standard solution to a suitable thin-layer chromatographic plate (see Chromatography (621)) coated with a 0.25-mm layer of chromatographic silica gel mixture, and allow to dry. Place the plate in an unlined chromatographic chamber, and develop the chromatograms in a solvent system consisting of a mixture of methanol and chloroform (85:15) until the solvent front has moved about 9 cm. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray the plate with a methanolic solution of 2′,7′-dichlorofluorescein (1 in 500), and examine the plate under long-wavelength UV light: the Rf values of the principal fluorescent spots obtained from the test solution correspond to those obtained from the Standard solution. Then spray the plate with a mixture of dehydrated alcohol, p-methoxybenzaldehyde, and sulfuric acid (90:5:5). Heat the plate at 100 °C for 10 minutes, and examine the chromatograms, in which the erythromycin appears as a black-to-purple spot: the Rf value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Dissolution (711)—
Medium: 0.05 M pH 6.8 phosphate buffer (see under Solutions in the section Reagents, Indicators, and Solutions); 900 mL.
Apparatus 2: 120 minutes.

Stock standard solution—Dissolve an accurately weighed quantity of USP Erythromycin RS in methanol to obtain a solution containing about 14 mg per mL. Dilute quantitatively with water to 50.0 mL, and mix. A working solution of about 0.56 mg of USP Erythromycin RS per mL.
Working standard solution—On the day of use, dilute 25.0 mL of Stock standard solution with water to 50.0 mL, and mix.

Test solution—After 120 minutes, withdraw a portion of the solution under test, filter, and dilute with Medium, if necessary, to obtain a solution having an estimated concentration of about 0.28 mg of erythromycin per mL.

Procedure—Transfer 5.0-mL portions of the Working standard solution to 25-mL volumetric flasks, one of which serves as a working standard blank. Similarly, transfer 5.0-mL portions of the Test solution to 25-mL volumetric flasks, one of which serves as a blank for that Test solution. To each of the flasks designated as a blank add 2.0 mL of 0.5 N sulfuric acid and to the remaining flasks add 2.0 mL of water. Allow to stand for 5 minutes with intermittent swirling. To all flasks add 15.0 mL of 0.25 N sodium hydroxide, dilute with Medium to volume, and mix. Heat the flasks in a water bath at 60 ± 0.5 °C for 5 minutes, and allow to cool. Using a suitable spectrophotometer, determine the absorbance of each solution, corrected for its blank solution, at the wavelength of maximum absorbance at about 236 nm. Determine the amount of C_{37}H_{67}NO_{13} dissolved from the Test solution in comparison with the solution obtained from the Working standard solution.

Tolerances—Not less than 75% (Q) of the labeled amount of C_{37}H_{67}NO_{13} is dissolved in 120 minutes.

Uniformity of dosage units (905): meet the requirements.
Loss on drying (731)—Dry about 100 mg of powdered tablets in a capillary-stoppered bottle in vacuum at 60 °C for 3 hours: it loses not more than 5.0% of its weight.

Assay—Proceed with Tablets as directed in the Assay under Erythromycin Tablets.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution B (%)</th>
<th>Solution C (%)</th>
<th>Flow Rate (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>95</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>35</td>
<td>65</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>45.1</td>
<td>0</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>60</td>
<td>0</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>60.1</td>
<td>95</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>68</td>
<td>95</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

[Note—The gradient was established on an HPLC system with a dwell volume of approximately 1.6 mL. The injection time can be adjusted relative to the start of a run to accommodate changes in dwell volume from one HPLC system to another to achieve the separation described.]
System suitability solution: 2 µg/mL each of USP Escitalopram Oxalate RS and USP Citalopram Related Compound D RS in Solution B

Standard solution: 0.5 mg/mL of USP Escitalopram Oxalate RS in Solution B

Sample solution: 0.5 mg/mL of Escitalopram Oxalate in Solution B

Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 237 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 45°C
Flow rate: See the gradient table above.
Injection size: 20 µL

System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 1.5 between escitalopram and citalopram related compound D, System suitability solution
Tailing factor: 0.8–3, Standard solution
Relative standard deviation: NMT 2.0%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percent of C₂₀H₂₁FN₂O · C₂H₂O₄ in the portion of Escitalopram Oxalate taken:

Result = \( \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \)

\( r_U = \) peak response of each impurity from the Sample solution
\( r_S = \) peak response of escitalopram from the Sample solution
\( C_S = \) concentration of the Standard solution (mg/mL)
\( C_U = \) concentration of the Sample solution (mg/mL)

Acceptance criteria: 98.0–102.0% on the anhydrous basis

**IMPURITIES**

**Inorganic Impurities**
- **Residue on Ignition (281):** NMT 0.1%
- **Heavy Metals, Method II (231):** NMT 20 ppm

**Organic Impurities**


System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 1.5 between escitalopram and citalopram related compound D, System suitability solution
Tailing factor: 0.8–3, Standard solution
Relative standard deviation: NMT 2.0%, Standard solution

Analysis
Sample: Sample solution
Calculate the percentage of each impurity in the portion of Escitalopram Oxalate taken:

Result = \( \left( \frac{r_U}{r_S} \right) \times (1/F) \times 100 \)

\( r_U = \) peak response of each impurity from the Sample solution
\( r_S = \) peak response of escitalopram from the Sample solution
\( F = \) relative response factor (see Impurity Table 1)

**Acceptance criteria**

**Individual impurities:** See Impurity Table 1.
Total impurities: NMT 0.5%

**Impurity Table 1**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-Dimethylaminobutyl Citalopram</td>
<td>0.40</td>
<td>0.34</td>
<td>0.2</td>
</tr>
<tr>
<td>Citalopram related compound A</td>
<td>0.50</td>
<td>0.79</td>
<td>0.1</td>
</tr>
<tr>
<td>Citalopram related compound B</td>
<td>0.74</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Citalopram related compound C</td>
<td>0.90</td>
<td>0.79</td>
<td>0.1</td>
</tr>
<tr>
<td>Citalopram related compound D</td>
<td>0.97</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Citalopram related compound E</td>
<td>1.1</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Individual unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.1</td>
</tr>
</tbody>
</table>

* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-5-(4-dimethylamino-1,3-dihydroisobenzofuran-5-carboxamide.
* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.
* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.
* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.
* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.
* 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.

**SPECIFIC TESTS**
- **Water Determination, Method I (921):** NMT 1.0%
- **Enantiomeric Purity**

Solution A: Dissolve 6.8 g of monobasic potassium phosphate in 250 mL of water, add 150 mL of 0.2 N sodium hydroxide, adjust with phosphoric acid or sodium hydroxide solution to a pH of 7.0, and dilute with water to 1 L.

Mobile phase: Acetonitrile and Solution A (3:17)

System suitability solution: 125 µg/mL each of USP R-Citalopram Oxalate RS and USP Escitalopram Oxalate RS in Mobile phase

Sample solution: 125 µg/mL of Escitalopram Oxalate in Mobile phase

Chromatographic system
(See Chromatography (621), System Suitability.)
Escitalopram Tablets

**DEFINITION**
Escitalopram Tablets contain an amount of escitalopram oxalate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of C₂₀H₂₁FN₂O₂.

**IDENTIFICATION**
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**
Buffer: 1.5 g of anhydrous sodium acetate and 0.4 mL of glacial acetic acid in 1 L of water. Adjust with 1 M sodium hydroxide to a pH of 5.2.
Mobile phase: Methanol, acetonitrile, and Buffer (33:7:60)
System suitability solution: 6.2 μg/mL of USP Citalopram Hydrobromide RS (equivalent to 5 μg/mL of citalopram) and 1 μg/mL of USP Citalopram Related Compound C RS in Mobile phase
Standard solution: 0.62 mg/mL of USP Citalopram Hydrobromide RS in Mobile phase (equivalent to 0.5 mg/mL of citalopram)
Sample solution: Transfer 10 Tablets to a suitable volumetric flask, add Buffer to 10% of the final volume, and shake vigorously for 10 min. Add methanol to 50% of the final volume, shake for 1 additional min, sonicate for 10 min, and dilute with Mobile phase to volume to obtain a solution having a concentration of about 0.5 mg/mL of escitalopram.

**Spectrometric conditions**
(See Spectrophotometry and Light-Scattering (851).)
Mode: UV-Vis
Analytical wavelength: 239 nm
Path length: 0.5 cm
Blank: Medium

**System suitability**
Samples: Standard solution 1, Standard solution 2, and Standard solution 3
Suitability requirements
Correlation coefficient: NMT 0.995, determined using Standard solution 1, Standard solution 2, and Standard solution 3, three replicates of each solution
Relative standard deviation: NMT 2.0%, determined using Standard solution 3, six replicates

**Analysis**
Samples: Standard solution 1, Standard solution 2, and Sample solution
Generate a calibration curve using the data from Standard solution 1, Standard solution 2, and Standard solution 3.
Determine the concentration, Cₗ, in mg/mL of citalopram hydrobromide in the Sample solution using the calibration curve.

Calculate the percentage of citalopram dissolved:
Result = \((Cₗ/L) \times (M₁/M₂)\) × V × 100

**Chromatographic system**
(See Chromatography (621), System Suitability.)