Levofloxacin Tablets. This monograph has been posted on the USP Pending Monograph Web page for review and public comments for at least 90 days. No comments were received. The SM1 Expert Committee has approved the monograph as an Authorized USP Pending Monograph.

The chromatographic procedure in the Assay is based on analyses performed with an Ace C18 brand of L1 column. The typical retention time for levofloxacin is about 1.9 min. The liquid chromatographic procedure in the test for Organic Impurities is based on analyses performed with the Hypersil BDS C18 brand of L1 column. The typical retention time for levofloxacin is about 17 min.

(SM1: B. Davani, M. Marques.)
Correspondence Number—C88216

Levofloxacin Tablets

v.1 Authorized May 1, 2011

DEFINITION
Levofloxacin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of levofloxacin (C18H20FN3O4).

IDENTIFICATION
• A. ULTRAVIOLET ABSORPTION (717)
  Standard solution and Sample solution: Prepare as directed in the test for Dissolution.
  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
• LEVOFLOXACIN
  Buffer: Dissolve 4 g of monobasic sodium phosphate dihydrate in 500 mL of water. Add 5 mL of triethylamine, and adjust with phosphoric acid to a pH of 5.9. Dilute with water to 1 L.
  Diluent: Acetonitrile and Buffer (50:50)
  Mobile phase: Methanol and Buffer (40:60)
  Standard solution: 0.05 mg/mL of USP Levofloxacin RS in Diluent. Pass through a suitable filter.
  Sample stock solution: 2.0 mg/mL of levofloxacin in Diluent from NLT 20 powdered Tablets. Pass through a suitable filter. Sonicate for 30 min with intermediate shaking to aid in dissolution.
  Sample solution: 0.04 mg/mL of levofloxacin in Diluent from the Sample stock solution
  Chromatographic system
  (See Chromatography (621), System Suitability.)
  Mode: LC
  Detector: UV 294 nm
  Column: 4.6-mm × 5-cm; 3-µm packing L1
  Column temperature: 40°C
  Flow rate: 1 mL/min
  Injection size: 5 µL
  Run time: 2 times the retention time of levofloxacin
  System suitability
  Sample: Standard solution
  Suitability requirements
  • Tailing factor: NMT 2.0
  • Relative standard deviation: NMT 2.0%
  Analysis
  Samples: Standard solution and Sample solution
  Calculate the percentage of the labeled amount of levofloxacin (C18H20FN3O4) in the portion of Tablets taken:
  \[
  \text{Result} = \frac{r_U}{r_S} \times \frac{(C/I)_{USP}}{(C/I)_{Sample}} \times 100
  \]
  \[r_U\] = peak response from the Sample solution
  \[r_S\] = peak response from the Standard solution

Acceptance criteria: 90%–110%

PERFORMANCE TESTS
• DISSOLUTION (711)
  Medium: 0.1 N hydrochloric acid; 900 mL
  Apparatus 1: 100 rpm
  Time: 30 min
  Detector: UV 293 nm
  Standard stock solution: 0.57 mg/mL of USP Levofloxacin RS in Medium
  Standard solution: Dilute the Standard stock solution with Medium to obtain solutions with final concentrations as given in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Tablet Strength (mg)</th>
<th>Final Concentration (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>5.7</td>
</tr>
<tr>
<td>500</td>
<td>5.7</td>
</tr>
<tr>
<td>750</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Sample solution: Pass a 10-mL portion through a filter of 0.45-µm pore size, and dilute with Medium to a concentration that is similar to the appropriate Standard solution.

Pathlength: 1 cm
Blank: Medium
Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of levofloxacin (C18H20FN3O4) dissolved:
\[
\text{Result} = \left( \frac{A_D}{A_S} \right) \times C_I \times D \times V \times (100/L)
\]
\[A_U\] = absorbance of the Sample solution
\[A_S\] = absorbance of the Standard solution
\[C_I\] = concentration of the Standard solution (mg/mL)
\[D\] = dilution factor for the Sample solution
\[V\] = volume of Medium, 900 mL
\[L\] = label claim (mg/Tablet)
Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin (C18H20FN3O4) is dissolved.

• UNIFORMITY OF DOSAGE UNITS (905): Meet the requirements

IMPURITIES
• ORGANIC IMPURITIES
  Buffer: Dissolve 4 g of ammonium acetate and 7 g of sodium perchlorate in 1 L of water. Add 2 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.6.
  Diluent: Acetonitrile and Buffer (20:80)
  Solution A: Acetonitrile and Buffer (2:98)
  Solution B: Acetonitrile and water (90:10)
  Mobile phase: See Table 2.

Table 2

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>15</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>35</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>45</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>46</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>55</td>
<td>90</td>
<td>10</td>
</tr>
</tbody>
</table>

Standard solution: 3 µg/mL of USP Levofloxacin RS and 2 µg/mL each of USP Levofloxacin Related Compounds A, B, and C RS in Diluent. Sonicate to aid in dissolution.

Sample solution: 1.0 mg/mL of levofloxacin in Diluent from NLT 20 powdered Tablets. Centrifuge a portion of the solution for about 10 min. Pass a portion through a suitable filter.
Sonicate for 20 min with intermediate shaking to aid in dissolution.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 294 nm
Column: 4.6-mm x 25-cm; 5-µm packing L1
Column temperature: 30°
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Sample: Standard solution
[Note—The Standard solution can be run for 1.5 times the retention time of levofloxacin.]
Suitability requirements
Tailing factor: NMT 2.0 for the levofloxacin peak
Relative standard deviation: NMT 10.0% for the levofloxacin peak
Resolution: NLT 5.0 between levofloxacin related compounds C and B
Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of each levofloxacin related compound in the portion of Tablets taken:

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

\( r_U \) = peak response of each levofloxacin related compound from the Sample solution
\( r_S \) = peak response of the corresponding impurity from the Standard solution
\( C_S \) = concentration of each levofloxacin related compound in the Standard solution (mg/mL)
\( C_U \) = nominal concentration of levofloxacin in the Sample solution (mg/mL)

Calculate the percentage of each individual unspecified impurity in the portion of Tablets taken:

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

\( r_U \) = peak response of each individual unspecified impurity from the Sample solution
\( r_S \) = peak response of levofloxacin from the Standard solution
\( C_S \) = concentration of USP Levofloxacin RS in the Standard solution (mg/mL)

\( C_U \) = nominal concentration of levofloxacin in the Sample solution (mg/mL)

Acceptance criteria: See Table 3.

### Table 3

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin related compound A†</td>
<td>0.59</td>
<td>0.2</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Levofloxacin related compound C‡</td>
<td>1.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Levofloxacin related compound B§</td>
<td>1.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>0.8</td>
</tr>
</tbody>
</table>

† (S)-9-Fluoro-2,3-dihydro-3-methyl-10-(piperazin-1-yl)-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid.
‡ (S)-Ethyl 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylate.
§ (S)-9,10-Difluoro-3-methyl-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylate.

**ADDITIONAL REQUIREMENTS**

- **Package and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **USP Reference Standards (11)**
  - USP Levofloxacin RS
  - USP Levofloxacin Related Compound A RS
  - USP Levofloxacin Related Compound B RS
  - USP Levofloxacin Related Compound C RS

This monograph has been developed under USP’s Pending Monographs Guideline and is not a USP–NF monograph.

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