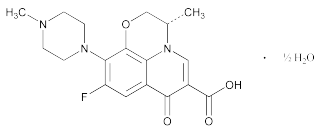
per mL, of levodopa ($C_9H_{11}NO_4$) in the portion of Tablets taken by the formula:

$$100C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Levodopa 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.

Levofloxacin



$C_{18}H_{20}FN_3O_4 \cdot {}^1/_2H_2O$ 370.38

7*H*-Pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-hydrate (2:1), (*S*)-;

(–)-(*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid, hemihydrate [138199-71-0].

Anhydrous [100986-85-41].

DEFINITION

Levofloxacin contains NLT 98.5% and NMT 102.0% of $C_{18}H_{20}FN_3O_4$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **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**

Solution A: 8.5 g/L of ammonium acetate, 1.25 g/L of cupric sulfate, pentahydrate, and 1.3 g/L of L-isoleucine in water

Mobile phase: Methanol and *Solution A* (3:7)

Standard solution: 1 mg/mL of USP Levofloxacin RS in *Mobile phase*

Sample solution: 1 mg/mL of Levofloxacin in *Mobile phase*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 360 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 0.8 mL/min

Injection size: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.5–1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{18}H_{20}FN_3O_4$ in the portion of Levofloxacin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of Levofloxacin 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 = concentration of Levofloxacin in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.2%. Use a platinum crucible.
- **Heavy Metals,** *Method II* ⟨231⟩**:** NMT 10 ppm

Organic Impurities

- **Procedure**

Solution A, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1 mg/mL of USP Levofloxacin RS in *Mobile phase*

Sensitivity solution: 0.3 µg/mL of USP Levofloxacin RS in *Mobile phase*

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 1.0%, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Levofloxacin taken:

$$\text{Result} = (r_U/r_S) \times (1/F) \times 100$$

r_U = peak area response of each impurity

r_S = peak area response of levofloxacin

F = relative response factor (see *Impurity Table 1*)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.5%. [NOTE—Do not include the D-isomer in the calculation for *Total impurities*.]

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
N-Desmethyl levofloxacin[a]	0.47	1.0	0.3
Diamine derivative[b]	0.52	0.9	0.3
Levofloxacin *N*-oxide[c]	0.63	1.1	0.3
9-Desfluoro levofloxacin[d]	0.73	1.0	0.3
Levofloxacin	1.0	—	—

[a] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(piperazin-1-yl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[b] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[c] (*S*)-4-(6-Carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7*H*-pyrido-[1,2,3-*de*][1,4]benzoxazine-10-yl)-1-methyl-piperazine-1-oxide.

[d] (*S*)-2,3-Dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[e] (*R*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

Impurity Table 1 *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
D-Isomer[e]	1.23	1.0	0.8
Any unknown impurity	—	1.0	0.1

[a] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(piperazin-1-yl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.
[b] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.
[c] (*S*)-4-(6-Carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7*H*-pyrido-[1,2,3-*de*][1,4]benzoxazine-10-yl)-1-methyl-piperazine-1-oxide.
[d] (*S*)-2,3-Dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.
[e] (*R*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

SPECIFIC TESTS

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
  Solvent: Methanol
  Sample solution: 5 mg/mL in *Solvent*
  Acceptance criteria: –92° to –106°, at 20°
- **WATER DETERMINATION,** *Method Ia* ⟨**921**⟩**:** 2.1%–2.7%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight and light-resistant containers. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Levofloxacin RS

Add the following:

▲Levofloxacin Oral Solution

DEFINITION

Levofloxacin Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$).

IDENTIFICATION

- **A.** 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**
  [NOTE—Protect the solutions of levofloxacin from light.]
  Diluent: Acetonitrile and water (18:82)
  Mobile phase: *Diluent* that contains 1 mL of trifluoroacetic acid in each 1000 mL of solution
  Standard solution: 102.5 µg/mL of USP Levofloxacin RS in *Diluent*
  System suitability solution: 102.5 µg/mL each of USP Levofloxacin RS and USP Levofloxacin Related Compound A RS in *Diluent*
  Sample solution: 102.5 µg/mL of levofloxacin in *Diluent* based on the label claim. [NOTE—Mix the solution well after equilibrating the solution for 4 h at room temperature while protected from light.]
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 294 nm
  Column: 4.6-mm × 15-cm; 3.5-µm packing L11
  Column temperature: 30°
  Flow rate: 0.7 mL/min
  Run time: 2.5 times the retention time of the levofloxacin peak
  Injection size: 20 µL
  System suitability
  Samples: *Standard solution* and *System suitability solution*
  Suitability requirements
  Resolution: NLT 1.9 between levofloxacin related compound A and levofloxacin, *System suitability solution*
  Relative standard deviation: NMT 2.0%, *Standard solution*
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response 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: 90.0%–110.0%

IMPURITIES

Organic Impurities

- **PROCEDURE**
  [NOTE—Protect the solutions of levofloxacin from light.]
  Diluent, Mobile phase, Standard solution, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of each individual impurity in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual 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)
F = relative response factor for each impurity (See *Impurity Table 1*)

Acceptance criteria
Individual impurities: See *Impurity Table 1*.

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
9-Desfluoro levofloxacin[a]	0.64	1.0	—*
Diamine derivative[b]	0.75	1.0	—*
Levofloxacin related compound A[c]	0.91	0.81	0.5
Levofloxacin	1.0	—	—

[a] (*S*)-2,3-Dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.
[b] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.
[c] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(piperazin-1-yl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carbocylic acid.
[d] (*S*)-4-(6-Carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7*H*-pyrido-[1,2,3-*de*][1,4]benzoxazine-10-yl)-1-methylpiperazine 1-oxide.
* Disregard this peak because this is a process impurity controlled for the drug substance.