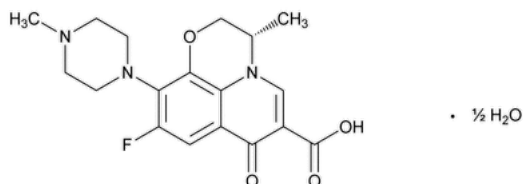


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Levofloxacin



$C_{18}H_{20}FN_3O_4 \cdot \frac{1}{2}H_2O$ 370.38

7H-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-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, hemihydrate CAS RN®: 138199-71-0; UNII: 6GNT3Y5LMF.
 Anhydrous CAS RN®: 100986-85-4.

DEFINITION

Levofloxacin contains NLT 98.0% and NMT 102.0% of $C_{18}H_{20}FN_3O_4$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 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

Buffer: 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 *Buffer* (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 levofloxacin ($C_{18}H_{20}FN_3O_4$) 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: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.2%. Use a platinum crucible.

Change to read:• **ORGANIC IMPURITIES, PROCEDURE 1**

[NOTE—*Procedure 1* is recommended if levofloxacin *N*-oxide is a potential organic impurity. *Procedure 2* and *Procedure 3* are recommended if levofloxacin related compound B is a potential organic impurity.]

▲ **Buffer,**▲ (ERR 1-Feb-2022) **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 response of each impurity

r_S = peak response of levofloxacin

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
<i>N</i> -Desmethyl levofloxacin ^a	0.47	1.0	0.3
Diamine derivative ^b	0.52	0.9	0.3
Levofloxacin <i>N</i> -oxide ^c	0.63	1.1	0.3
9-Desfluoro levofloxacin ^d	0.73	1.0	0.3
Levofloxacin	1.0	—	—
<i>D</i> -Isomer ^e	1.23	1.0	0.8
Any unknown impurity	—	1.0	0.1
Total Impurities	—	—	0.5 ⁺

* Do not include the *D*-isomer in the calculation for total impurities.

^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.

• **ORGANIC IMPURITIES, PROCEDURE 2**

[NOTE—Solutions of levofloxacin are not stable in light; use amber bottles.]