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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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2024)

ASSAY

Change to read:

• **Procedure**

[Note—Protect the solutions of levofloxacin from light.]

Diluent: Acetonitrile and water (18:82)

Mobile phase: Add 1 mL of trifluoroacetic acid to each 1000 mL of *Diluent*

System suitability solution: 0.1025 mg/mL each of USP Levofloxacin RS and USP Levofloxacin Related Compound A RS in *Diluent*

Standard solution: 0.1025 mg/mL of USP Levofloxacin RS in *Diluent*

Sample solution: ▲Nominally▲ (USP 1-May-2024) 0.1025 mg/mL of levofloxacin prepared 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. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2024)

Column: 4.6-mm × 15-cm; 3.5-µm packing L11

Column temperature: 30°

Flow rate: 0.7 mL/min

Injection volume: 20 µL

Run time: ▲NLT▲ (USP 1-May-2024) 2.5 times the retention time of levofloxacin

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.9 between levofloxacin related compound A and levofloxacin, *System suitability solution*

▲**Tailing factor:** NMT 2.0, *Standard solution*▲ (USP 1-May-2024)

Relative standard deviation: NMT ▲1.0%▲ (USP 1-May-2024) , *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 ▲of levofloxacin▲ (USP 1-May-2024) from the *Sample solution*

r_S = peak response ▲of levofloxacin▲ (USP 1-May-2024) 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

Change to read:

• **Organic Impurities**

[Note—Protect the solutions of levofloxacin from light.]

Diluent, Mobile phase, ▲ (USP 1-May-2024) **System suitability solution, Sample solution,** and **Chromatographic system** ▲ (USP 1-May-2024) **:** Proceed as directed in the *Assay*.

▲**Standard solution:** 0.000205 mg/mL of USP Levofloxacin RS in *Diluent*

Sensitivity solution: 0.1025 µg/mL of USP Levofloxacin RS from the *Standard solution* in *Diluent*

System suitability

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

[Note—The relative retention times in *Table 1* are provided as information that could aid in peak assignment.]

Table 1

Name	Relative Retention Time
9-Desfluoro levofloxacin[a]	0.64
Levofloxacin diamine derivative[b]	0.75
Levofloxacin related compound A	0.91
Levofloxacin	1.0
Levofloxacin *N*-oxide[c]	1.55

[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*)-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.

Suitability requirements

Resolution: NLT 1.9 between levofloxacin related compound A and levofloxacin, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution* ▲ (USP 1-May-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each ▲degradation product▲ (USP 1-May-2024) 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 ▲degradation product▲ (USP 1-May-2024) 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 (see *Table 2*)

▲**Acceptance criteria:** See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Levofloxacin related compound A	0.81	0.5

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Levofloxacin *N*-oxide	0.93	0.5
Any unspecified degradation product	1.0	0.2
Total degradation products	—	1.0

▲ (USP 1-May-2024)

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests For Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/mL, and the total combined molds and yeast count does not exceed 10^1 cfu/mL. It also meets the requirement for absence of *Escherichia coli*.

• **Deliverable Volume ⟨698⟩:** Meets the requirements

• **pH ⟨791⟩:** 5.0–6.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Protect from light. Store at controlled room temperature.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Levofloxacin RS

▲▲ (USP 1-May-2024)

USP Levofloxacin Related Compound A RS

▲*S*)-9-Fluoro-3-methyl-10-(piperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.▲ (USP 1-May-2024)

$C_{17}H_{18}FN_3O_4$ ▲347.35▲ (USP 1-May-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LEVOFLOXACIN ORAL SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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