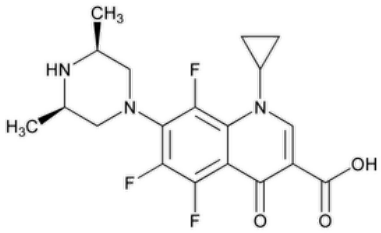
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2022
Document Type: USP Monographs
DocId: GUID-89C55335-5F85-475A-AF00-C3C0F8C225DD_6_en-US
DOI: https://doi.org/10.31003/USPNF_M58770_06_01
DOI Ref: oyx0o

Orbifloxacin



$C_{19}H_{20}F_3N_3O_3$ 395.38

1-Cyclopropyl-7-(*cis*-3,5-dimethyl-1-piperazinyl)-5,6,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid CAS RN®: 113617-63-3; UNII: 660932TPY6.

» Orbifloxacin contains not less than 98.5 percent and not more than 101.5 percent of $C_{19}H_{20}F_3N_3O_3$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers. Store at room temperature.

USP Reference standards ⟨11⟩—

USP Orbifloxacin RS

Identification—

A: *Spectroscopic Identification Tests* ⟨197⟩, *Infrared Spectroscopy: 197K*

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Change to read:

C: ▲*X-Ray Powder Diffraction* ⟨941⟩—▲ (CN 1-May-2022) The X-ray diffraction pattern conforms to that of USP Orbifloxacin RS, similarly determined.

Microbial enumeration tests ⟨61⟩—The total combined molds and yeasts count does not exceed 100 cfu per g.

pH ⟨791⟩**:** between 6.5 and 7.8, in a solution containing 10 mg per mL.

Water Determination, *Method Ic* ⟨921⟩**:** between 1.5% and 2.9%.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Related compounds—

Buffer, Mobile phase, System suitability preparation, Standard preparation, and *Chromatographic system*— Prepare as directed in the *Assay.*

Standard solution—Dilute, quantitatively with *Buffer,* the *Standard preparation* to obtain a solution having a known concentration of about 0.00004 mg per mL.

Test solution—Transfer about 40 mg of Orbifloxacin, accurately weighed, to a 200-mL volumetric flask, dissolve in and dilute with *Buffer* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Inject the *Buffer* as directed for *Procedure* to verify that there are no interfering peaks.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the percentage of related compounds in the portion of Orbifloxacin taken by the formula:

$$20{,}000(C_S)(r_i/r_S)(1/F)(1/W)$$

in which C_S is the concentration, in mg per mL, of orbifloxacin in the *Standard solution;* r_i is the peak area response for each impurity obtained from the *Test solution;* r_S is the peak area response for the orbifloxacin peak obtained from the *Standard solution; F* is the relative response factor for each impurity, as presented in *Table 1*; and *W* is the sample weight taken to prepare the *Test solution* (mg).

Table 1

Component/Impurity	Approximate Relative Retention Time	Relative Response Factor *(F)*	Limit %
cis, cis-1-Cyclopropyl-5,7-bis(3,5-dimethyl-1-piperazinyl)-6,8-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid	0.5	0.36	NMT 0.2
cis-1-Cyclopropyl-7-(3,5-dimethyl-1-piperazinyl)-5,6,8-trifluoro-4(1*H*)-quinolinone	0.65	0.27	NMT 0.2
7-[(2-Aminopropyl)amino]-1-cyclopropyl-5,6-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid	0.75	0.49	NMT 0.2
Orbifloxacin	1.0	1.00	—
1-Cyclopropyl-7-(3,5-dimethyl-1-piperazinyl)-6,8-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid	1.4	0.84	NMT 0.2
cis-1-Cyclopropyl-7-(3,5-dimethyl-1-piperazinyl)-6,8-difluoro-1,4-dihydro-5-hydroxy-4-oxo-3-quinolinecarboxylic acid	2.7	0.73	NMT 0.2
cis-1-Cyclopropyl-5-(3,5-dimethyl-1-piperazinyl)-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid	3.6	0.11	NMT 0.2
1-Cyclopropyl-5,6,7,8-tetrafluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid	6.8	0.16	NMT 0.2
Unknown	—	1.0	—
Total known and unknown	—	—	NMT 0.4

Assay—

Buffer—In a 2-L flask, dissolve about 11.8 g of sodium citrate in 1600 mL of water, and mix. Add 180 mL of acetic acid, and mix. Adjust with 6 N sodium hydroxide to a pH of 3.5, dilute with water to about 2 L, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer,* methanol, and dioxane (86:11:4). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock preparation—Dissolve in *Buffer* an accurately weighed quantity of USP Orbifloxacin RS to obtain a solution having a known concentration of about 0.2 mg per mL.

Standard preparation—Accurately transfer a quantity of *Standard stock preparation,* and dilute with *Buffer* to obtain a solution having a known concentration of about 0.02 mg per mL.

System suitability preparation—Dissolve about 40 mg of methyl 4-aminobenzoate in 2 mL of methanol, and dilute with *Buffer* to 200 mL. Pipet 10.0 mL of this solution and 10.0 mL of *Standard stock preparation* into a 100-mL volumetric flask. Dilute with *Buffer* to volume, and mix.

Assay preparation—Transfer about 40 mg of Orbifloxacin accurately weighed, to a 200-mL volumetric flask, dissolve in and dilute with *Buffer* to volume, and mix. Dilute with *Buffer* an aliquot of the resulting solution to obtain a solution having a known concentration of about 0.02 mg per mL.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 290-nm detector and 4.6-mm × 3.0-cm column that contains 3-µm packing L1. The flow rate is about 1.0 mL per minute. Prior to injecting the *System suitability preparation,* flush the column with approximately 50 mL of a mixture of acetonitrile and water (9:1). Chromatograph the *System suitability preparation,* and record the peak response as directed for *Procedure:* the relative retention times are about 1.3 for methyl 4-aminobenzoate and 1.0 for orbifloxacin; the resolution, *R,* between methyl 4-aminobenzoate and orbifloxacin is not less than 2; the tailing factor is not more than 1.8; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatographs, and measure the area responses for the major peaks. Calculate the quantity, in mg, of $C_{19}H_{20}F_3N_3O_3$ in the portion of Orbifloxacin taken by the formula:

$$2000C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Orbifloxacin RS in the *Standard preparation;* and r_U and r_S are the peak area responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
ORBIFLOXACIN	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 34(2)

Current DocID: GUID-89C55335-5F85-475A-AF00-C3C0F8C225DD_6_en-US
DOI: https://doi.org/10.31003/USPNF_M58770_06_01
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