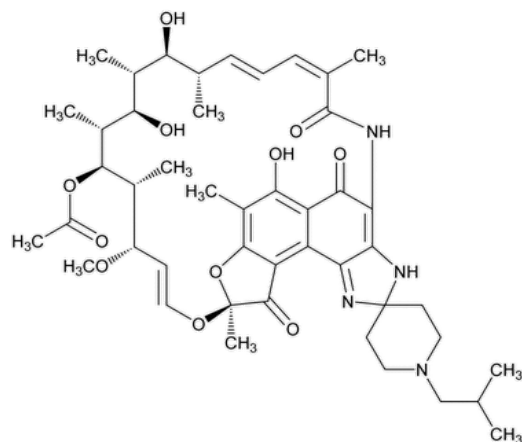


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Rifabutin

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$C_{46}H_{62}N_4O_{11}$ 847.02

(9S,12E,14S,15R,16S,17R,18R,19R,20S,21S,22E,24Z)-6,18,20-Trihydroxy-1'-isobutyl-14-methoxy-7,9,15,17,19,21,25-heptamethyl-5,10,26-trioxo-3,5,9,10-tetrahydrospiro[9,4-(epoxypentadeca[1,11,13]trienimino)-2H-furo[2',3':7,8]naphtho[1,2-d]imidazole-2,4'-piperidin]-16-yl acetate CAS RN®: 72559-06-9.

DEFINITION

Rifabutin contains NLT 950 µg/mg and NMT 1020 µg/mg of rifabutin ($C_{46}H_{62}N_4O_{11}$), 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

Solution A: 13.6 g/L of [monobasic potassium phosphate](#)

Mobile phase: [Acetonitrile](#) and *Solution A* (50:50). Adjust by dropwise addition of [2 N sodium hydroxide](#) to a pH of 6.5 ± 0.1 .

System suitability solution: Dissolve about 10 mg of Rifabutin in 2 mL of [methanol](#), add 1 mL of [2 N sodium hydroxide](#), and allow to stand for 4 min. Add 1 mL of [2 N hydrochloric acid](#), and dilute with *Mobile phase* to 50 mL. [NOTE—Portions of this solution may be stored in the frozen state for future use.]

Standard solution: 0.5 mg/mL of [USP Rifabutin RS](#) prepared as follows. Transfer an amount of [USP Rifabutin RS](#) to a suitable volumetric flask. Add [acetonitrile](#) to fill 10% of the volume of the flask, and dilute with *Mobile phase* to volume.

Sample solution: 0.5 mg/mL of Rifabutin prepared as follows. Transfer an amount of Rifabutin to a suitable volumetric flask. Add [acetonitrile](#) to fill 10% of the volume of the flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing [L7](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of the rifabutin peak

System suitability

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

[NOTE—The chromatogram of the *System suitability solution* exhibits a major peak for a degradant, two minor peaks for degradants, and a major peak for rifabutin at relative retention times of about 0.5, 0.6, 0.8, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.3 between the degradant peak eluting at a relative retention time of about 0.8 and the rifabutin peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of rifabutin ($C_{46}H_{62}N_4O_{11}$) in the portion of Rifabutin taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Rifabutin RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Rifabutin in the *Sample solution* (mg/mL)

P = potency of [USP Rifabutin RS](#) (µg/mg)

Acceptance criteria: 950–1020 µg/mg on the anhydrous basis

IMPURITIES

• ORGANIC IMPURITIES, PROCEDURE 1: LIMIT OF *N*-ISOBUTYLPYPERIDONE

Diluent: [Chloroform](#) and [methanol](#) (1:1)

Standard solution 1: 0.1 mg/mL of *N*-isobutylpiperidone in *Diluent*

Standard solution 2: 0.05 mg/mL of *N*-isobutylpiperidone in *Diluent*

Standard solution 3: 0.02 mg/mL of *N*-isobutylpiperidone in *Diluent*

Standard solution 4: 0.01 mg/mL of *N*-isobutylpiperidone in *Diluent*

Standard solution 5: 0.005 mg/mL of *N*-isobutylpiperidone in *Diluent*

Sample solution: 10 mg/mL of Rifabutin in *Diluent*

Chromatographic system

(See [Chromatography \(621\)](#), [General Procedures](#), [Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: [Hexanes](#) and [acetone](#) (100:30)

Analysis: Apply portions of the *Sample solution* and the *Standard solutions* to a suitable TLC plate (see [Chromatography \(621\)](#)) coated with *Adsorbent*. Develop the chromatograms in the *Developing solvent system*, contained in an equilibrated unlined chromatographic chamber, until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chromatographic chamber, allow the plate to air-dry, and place it in an iodine vapor chamber until the spots are visible (about 5 min). Remove the plate from the chamber, spray the plate with [starch TS](#), and examine the plate.

Acceptance criteria: NMT 0.5%. No spot from the *Sample solution* at an R_f value corresponding to that of *N*-isobutylpiperidone is more intense than that of the principal spot observed from *Standard solution 2*.

Change to read:

• ORGANIC IMPURITIES, PROCEDURE 2

Solution A: 0.1% (v/v) [triethylamine](#) in [water](#)

Solution B: [Acetonitrile](#) and *Solution A* (20:80). Adjust with [trifluoroacetic acid](#) to a pH of 2.5.

Solution C: [Acetonitrile](#) and *Solution A* (90:10). Adjust with [trifluoroacetic acid](#) to a pH of 2.5.

Mobile phase: See [Table 1](#).

Table 1