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## Rifabutin Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click [www.uspnf.com/rb-rifabutin-caps-20231229](http://www.uspnf.com/rb-rifabutin-caps-20231229).

### DEFINITION

Rifabutin Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of rifabutin ( $C_{46}H_{62}N_4O_{11}$ ).

### IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy:** 197U

**Standard solution:** 20 µg/mL of [USP Rifabutin RS](#) in [methanol](#), prepared with the aid of sonication. Pass through a filter of 0.5-µm or finer pore size.

**Sample solution:** Nominally 20 µg/mL of rifabutin prepared as follows. Suspend a quantity of Capsule contents, equivalent to 200 mg of rifabutin, in 20 mL of [methanol](#). Sonicate for 5 min, and pass through a suitable filter of 0.5-µm or finer pore size. Dilute a portion of the filtrate with [methanol](#) to obtain a solution containing 20 µg/mL of rifabutin.

**Acceptance criteria:** Meet the requirements

- **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

**Change to read:**

- **PROCEDURE**

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

**Mobile phase:** [Acetonitrile](#) and *Solution A* (50:50). Adjust with ▲2 N [sodium hydroxide](#)▲ (RB 1-Jan-2024) to a pH of  $6.5 \pm 0.1$ . Pass through a suitable filter of 0.5-µm or finer pore size.

**System suitability solution:** Dissolve 10 mg of Rifabutin in 2 mL of [methanol](#), add 1 mL of ▲2 N [sodium hydroxide](#)▲ (RB 1-Jan-2024), and allow to stand for 4 min. Add 1 mL of ▲2 N [hydrochloric acid](#)▲ (RB 1-Jan-2024), 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:** Nominally 0.5 mg/mL of rifabutin prepared as follows. Remove the contents of NLT 20 Capsules, weigh, and determine the average weight of the Capsule contents. Transfer a portion of the powder, equivalent to 25 mg of rifabutin, to a 50-mL volumetric flask, add 5 mL of [acetonitrile](#), and dilute with *Mobile phase* to volume. Pass through a suitable filter of 0.5-µm or finer pore size.

### 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 rifabutin peak and the degradant peak eluting at a relative retention time of about 0.8, *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 rifabutin ( $C_{46}H_{62}N_4O_{11}$ ) in the portion of Capsules taken:

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

$r_U$  = peak response of rifabutin from the *Sample solution*

$r_S$  = peak response of rifabutin from the *Standard solution*

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

$C_U$  = nominal concentration of rifabutin in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

#### PERFORMANCE TESTS

##### • DISSOLUTION

**Medium:** 0.01 N [hydrochloric acid](#); 900 mL

**Apparatus 1:** 100 rpm

**Time:** 45 min

**Standard solution:** A known concentration of [USP Rifabutin RS](#) in *Medium*

**Sample solution:** A filtered portion of the solution under test, suitably diluted with *Medium* to a concentration similar to that of the *Standard solution*, taking into account its designated potency.

##### Instrumental conditions

**Mode:** UV

**Analytical wavelength:** 280 nm

##### Analysis

**Samples:** *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of rifabutin ( $C_{46}H_{62}N_4O_{11}$ ) dissolved:

$$(A_U/A_S) \times C_S \times D \times (V/L) \times 100$$

$A_U$  = absorbance of the *Sample solution*

$A_S$  = absorbance of the *Standard solution*

$C_S$  = concentration of the *Standard solution* (mg/mL)

$D$  = dilution factor of the *Sample solution*, if needed

$V$  = volume of *Medium*, 900 mL

$L$  = label claim (mg/Capsule)

**Tolerances:** NLT 75% (Q) of the labeled amount of rifabutin ( $C_{46}H_{62}N_4O_{11}$ ) is dissolved.

#### IMPURITIES

##### Change to read:

##### • ORGANIC IMPURITIES

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

**Solution B:** [Acetonitrile](#) and *Solution A* (40:60). Adjust with 2 N [sodium hydroxide](#) to a pH of 6.5.

**Solution C:** [Acetonitrile](#) and *Solution A* (70:30). Adjust with 2 N [sodium hydroxide](#) to a pH of 6.5.

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

Table 1