Summary

The disclosure provides pharmaceutical formulations that contain high concentrations of rifabutin. Preferred compositions of the disclosure comprise a rifabutin powder formulated in water, a solvent and an acid. The inventive combination allows dissolution of rifabutin at high concentration. The formulated solution may be diluted without restriction in order to render a composition suitable for a desired route of administration.

Formulations of the disclosure allow delivery of effective amounts of rifabutin by routes of administration that are not possible with prior rifabutin-containing compositions. For example, formulations of the disclosure enable rifabutin to be provided parenterally, including intravenously or by inhalation. In addition, formulations of the disclosure obviate the need to lyophilize rifabutin prior to reconstituting it for administration, a rather costly process.

In one aspect, the present disclosure provides a rifabutin formulation produced from a rifabutin powder in the presence of an acid, water, and a solvent suitable to promote dissolution of the rifabutin, wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic, and wherein the formulation has a rifabutin concentration between 50 mg/mL and 250 mg/mL at room temperature. In another aspect, the present disclosure provides a method of preparing the formulation as described herein, the method comprising: preparing a solution comprising a solvent, water and an acid; and adding said solution to rifabutin powder, thereby causing the rifabutin to dissolve in the solution, wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), and wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic. In yet another aspect, the present disclosure provides a method of preparing the formulation as described herein, the method comprising: preparing a solution comprising water and an acid; and adding said solution to a rifabutin solution in a solvent, thereby producing an aqueous rifabutin formulation, wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), and wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic.

In another example of the disclosure, rifabutin is prepared as a powder with a shelf-life equivalent to that of the rifabutin active pharmaceutical ingredient (API). As detailed below, rifabutin formulations of the disclosure preferably comprise rifabutin powder dissolved in an organic solvent.

According to the disclosure, highly concentrated rifabutin formulations are rapidly obtained from any rifabutin API and used as such or further diluted ad libitum with sterile water or pharmaceutically-acceptable solutions. Formulations of the disclosure are useful for treating a variety of conditions caused by or associated with bacterial infections, such as, but not limited to,

Claims

What is claimed is:

1. A rifabutin formulation produced from a rifabutin powder in the presence of an acid, water, and a solvent suitable to promote dissolution of the rifabutin, wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic, and wherein the formulation has a rifabutin concentration between 50 mg/mL and 250 mg/mL at room temperature.

2. The formulation of claim 1, wherein the ratio of rifabutin to solvent w/v is about 1:2.

3. The formulation of claim 1, wherein the solvent is DMI or transcutol HP.

4. The formulation of claim 1, wherein the solvent to water ratio v/v is from 1:1 to 1:2.

5. The formulation of claim 1, wherein the acid is acetic acid or D-glucuronic acid.

6. The formulation of claim 1, wherein the rifabutin to acid molar ratio is about 1:1.

7. The formulation of claim 1, further comprising sterile water or pharmaceutically-acceptable solutions to dilute the formulation in order to produce a composition suitable for a desired route of administration.

8. A method of preparing the formulation of claim 1, the method comprising:

preparing a solution comprising a solvent, water and an acid; and

adding said solution to rifabutin powder, thereby causing the rifabutin to dissolve in the solution,

wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), and

wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic.

9. The method of claim 8, wherein the solvent is selected from dimethyl isosorbide (DMI) and -diethylene glycol monoethyl ether (transcutol HP).

10. The method of claim 8, wherein the acid is selected from acetic acid and D-glucuronic acid.

11. A method of preparing the formulation of claim 1, the method comprising:

preparing a solution comprising water and an acid; and

adding said solution to a rifabutin solution in a solvent, thereby producing an aqueous rifabutin formulation,

wherein the solvent is selected from the group consisting of: dimethylacetamide (DMA), diethylene glycol monoethyl ether (transcutol HP), and dimethyl isosorbide (DMI), and

wherein the acid is selected from the group consisting of: hydrochloric, methanesulfonic, phosphoric, L-tartaric, D-glucuronic, L-malic, D-gluconic, L-lactic, and acetic

12. The method of claim 11, wherein the solvent is selected from dimethyl isosorbide (DMI) and diethylene glycol monoethyl ether (transcutol HP).

13. The method of claim 11, wherein the acid is selected from acetic acid or D-glucuronic acid.

14. Use of the formulation of claim 1 in the manufacture of a medicament for treating a bacterial infection in a subject, wherein the rifabutin is to be administered in an injectable formulation or by inhalation.

15. The formulation of claim 7, wherein the desired route of administration is by injection.

16. The formulation of claim 7, wherein the desired route of administration is by inhalation.