CLAIMS

What is claimed is:

1. A sterile liquid formulation of aprepitant for injection, comprising:
an aqueous single phase solvent system comprising water, a primary co-solvent, a surfactant, and a secondary co-solvent;
wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to solubilization of aprepitant;
wherein the secondary co-solvent is present in an amount of equal or less than 6 volume % of the water and the primary co-solvent together; and
wherein aprepitant is dissolved in the aqueous single phase solvent system at a concentration of at least 5 mg/ml.

2. The sterile liquid formulation of claim 1, wherein the primary co-solvent is a short-chain alcohol.

3. The sterile liquid formulation of claim 2, wherein the short-chain alcohol is ethanol.

4. The sterile liquid formulation of claim 1, wherein the surfactant is a nonionic surfactant.

5. The sterile liquid formulation of claim 4, wherein the non-ionic surfactant is a polysorbate.

6. The sterile liquid formulation of claim 1, wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

7. The sterile liquid formulation of claim 6, wherein the secondary co-solvent is a short-chain polyethylene glycol and is present in an amount of equal or less than 3 volume %.

8. The sterile liquid formulation of claim 6, wherein the secondary co-solvent is dimethylacetamide and is present in an amount of equal or less than 1 volume %.

9. The sterile liquid formulation of claim 1, wherein the primary co-solvent is ethanol, the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide, and wherein the surfactant is a polysorbate.

10. The sterile liquid formulation of claim 1, wherein the secondary co-solvent is omitted from the sterile liquid formulation.

11. A kit for preparation of a sterile liquid formulation of aprepitant for injection, the kit comprising:

(a) a first container that includes a solvent system comprising a primary co-solvent, a surfactant, and an optional secondary co-solvent;

wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to complete solubilization of aprepitant in the solvent system;

wherein the optional secondary co-solvent is present in an amount of equal or less than 30 vol% of the primary co-solvent and the surfactant together;

aprepitant at a concentration of at least 9 mg/ml;

(b) a second container that includes a sterile aqueous diluent in an amount sufficient to dilute the aprepitant to a concentration of at least 5 mg/ml; and

wherein the non-aqueous solvent system and the sterile aqueous diluent are present in an amount such that the aprepitant at the concentration of at least 5 mg/ml is completely soluble and stable in the sterile liquid formulation.

12. The kit of claim 11 wherein the primary co-solvent is a short-chain alcohol, and wherein the surfactant is a non-ionic surfactant.

13. The kit of claim 11 wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

14. The kit of claim 11 wherein the sterile aqueous diluent is water.

15. A method of increasing solubility and stability of aprepitant in an aqueous solution, the method comprising:

preparing an aqueous single phase solvent system comprising water, a primary co-solvent, and a surfactant, wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to solubilization of aprepitant;

dissolving aprepitant in a secondary co-solvent to form a concentrated aprepitant solution having an aprepitant concentration of at least 5mg/ml in the secondary co-solvent;

combining the concentrated aprepitant solution with the aqueous single phase solvent system to thereby form an aprepitant formulation with increased solubility and stability for aprepitant.

16. The method of claim 15 wherein the primary co-solvent is a short-chain alcohol.

17. The method of claim 15 wherein the surfactant is a nonionic surfactant.

18. The method of claim 15 wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

19. The method of claim 15 wherein aprepitant formulation contains at least 5 mg/ml aprepitant.

20. The method of claim 15 wherein aprepitant in the aprepitant formulation remains in solution for at least one month when stored at 40 °C and 75% relative humidity.

CLAIMS

What is claimed is:

1. A sterile liquid formulation of aprepitant for injection, comprising:
   an aqueous single phase solvent system comprising water, a primary co-solvent, a surfactant, and a secondary co-solvent;
   wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to solubilization of aprepitant;
   wherein the secondary co-solvent is present in an amount of equal or less than 6 volume % of the water and the primary co-solvent together; and
   wherein aprepitant is dissolved in the aqueous single phase solvent system at a concentration of at least 5 mg/ml,
   wherein the aprepitant formulation is formulated to be chemically stable and remain in solution for at least one month when stored at 40 degrees Celsius and 75% relative humidity.

2. The sterile liquid formulation of claim 1, wherein the primary co-solvent is a short-chain alcohol.

3. The sterile liquid formulation of claim 2, wherein the short-chain alcohol is ethanol.

4. The sterile liquid formulation of claim 1, wherein the surfactant is a nonionic surfactant.

5. The sterile liquid formulation of claim 4, wherein the non-ionic surfactant is a polysorbate.

6. The sterile liquid formulation of claim 1, wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

7. The sterile liquid formulation of claim 6, wherein the secondary co-solvent is a short-chain polyethylene glycol and is present in an amount of equal or less than 3 volume %.

8. The sterile liquid formulation of claim 6, wherein the secondary co-solvent is dimethylacetamide and is present in an amount of equal or less than 1 volume %.

9. The sterile liquid formulation of claim 1, wherein the primary co-solvent is ethanol, the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide, and wherein the surfactant is a polysorbate.

10. The sterile liquid formulation of claim 1, wherein the secondary co-solvent is omitted from the sterile liquid formulation.

11. A kit for preparation of a sterile liquid formulation of aprepitant for injection, the kit comprising:

(a) a first container that includes a solvent system comprising a primary co-solvent, a surfactant, and an optional secondary co-solvent;

wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to complete solubilization of aprepitant in the solvent system;

wherein the optional secondary co-solvent is present in an amount of equal or less than 30 vol% of the primary co-solvent and the surfactant together;

aprepitant at a concentration of at least 9 mg/ml;

(b) a second container that includes a sterile aqueous diluent in an amount sufficient to dilute the aprepitant to a concentration of at least 5 mg/ml; and

wherein the non-aqueous solvent system and the sterile aqueous diluent are present in an amount such that the aprepitant at the concentration of at least 5 mg/ml is completely soluble and stable in the sterile liquid formulation,

wherein the aprepitant formulation is formulated to be chemically stable and remain in solution for at least one month when stored at 40 degrees Celsius and 75% relative humidity.

12. The kit of claim 11 wherein the primary co-solvent is a short-chain alcohol, and wherein the surfactant is a non-ionic surfactant.

13. The kit of claim 11 wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

14. The kit of claim 11 wherein the sterile aqueous diluent is water.

15. A method of increasing solubility and stability of aprepitant in an aqueous solution, the method comprising:

preparing an aqueous single phase solvent system comprising water, a primary co-solvent, and a surfactant, wherein the primary co-solvent and the surfactant are present in a synergistic ratio with respect to solubilization of aprepitant;

dissolving aprepitant in a secondary co-solvent to form a concentrated aprepitant solution having an aprepitant concentration of at least 5mg/ml in the secondary co-solvent;

combining the concentrated aprepitant solution with the aqueous single phase solvent system to thereby form an aprepitant formulation with increased solubility and stability for aprepitant,

wherein the aprepitant formulation is formulated to be chemically stable and remain in solution for at least one month when stored at 40 degrees Celsius and 75% relative humidity.

16. The method of claim 15 wherein the primary co-solvent is a short-chain alcohol.

17. The method of claim 15 wherein the surfactant is a nonionic surfactant.

18. The method of claim 15 wherein the secondary co-solvent is a short-chain polyethylene glycol or dimethylacetamide.

19. The method of claim 15 wherein aprepitant formulation contains at least 5 mg/ml aprepitant.

20. The method of claim 15 wherein aprepitant in the aprepitant formulation remains in solution for at least one month when stored at 40 °C and 75% relative humidity.