CLAIM

1. A pharmaceutical composition comprising apixaban and a pharmaceutically acceptable diluent or carrier, wherein:

as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the pharmaceutical composition dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate;

the apixaban comprises crystalline apixaban particles; and

the crystalline apixaban particles have a D90 equal to or less than about 89 μm.

2. A pharmaceutical composition comprising apixaban and a pharmaceutically acceptable diluent or carrier,

wherein apixaban comprises crystalline apixaban particles, and

wherein the crystalline apixaban particles have a D90 equal to or less than about 89 μm as measured by laser light scattering.

3. The composition as defined in claim 2, wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37°C, at least 77% of apixaban in the pharmaceutical composition dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH of 6.8 containing 0.05% sodium lauryl sulfate.

4. A solid pharmaceutical composition comprising apixaban and a pharmaceutically acceptable diluent or carrier,

wherein raw materials from which the solid pharmaceutical composition is prepared comprise crystalline apixaban particles having a D90 equal to or less than about 89 μm as measured by laser light scattering, and

wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the solid pharmaceutical composition dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate.

5. The composition as defined in claim 4, wherein the raw materials are granulated during preparation of the solid pharmaceutical composition.

6. The composition as defined in claim 5, wherein the raw materials are granulated by dry granulation.

7. The composition as defined in any one of claims 1 to 6, wherein the D90 is equal to or less than 85 μm as measured by laser light scattering.

8. The composition as defined in any one of claims 1 to 6, wherein the D90 is equal to or less than 50 μm as measured by laser light scattering.

9. The composition as defined in any one of claims 1 to 6, wherein the D90 is equal to or less than 30 μm as measured by laser light scattering.

10. The composition as defined in any one of claims 1 to 6, wherein the D90 is equal to or less than 25 μm as measured by laser light scattering.

11. The composition as defined in any one of claims 1 to 10, wherein the pharmaceutical composition comprises from about 2.5 mg to about 5 mg of apixaban.

12. The composition as defined in any one of claims 1 to 10 comprising 2.5 mg of apixaban.

13. The composition as defined in any one of claims 1 to 10 comprising 5 mg of apixaban.

14. The composition as defined in any one of claims 1 to 13, wherein said composition comprises Form N-1 of apixaban.

15. The composition as defined in any one of claims 1 to 14, further comprising from about 1% to about 2 % by weight of a surfactant.

16. The composition as defined in claim 15, wherein the surfactant is sodium lauryl sulfate.

17. The composition as defined in any one of claims 1 to 16 in the form of a tablet or capsule.

18. The composition as defined in any one of claims 1 to 16 in the form of a tablet.

19. A process for preparing a tablet comprising about 2.5 mg to about 5 mg of apixaban and a pharmaceutically acceptable diluent or carrier, the process comprising:
blending raw materials comprising crystalline apixaban particles having a D90 equal to or less than about 89 μm as measured by laser light scattering; and
granulating,
wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the tablet dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate.

20. The process of claim 19, comprising the steps of:
(1) blending raw materials comprising crystalline apixaban particles prior to granulation;
(2) granulating the raw materials from the step (1) using a wet or dry granulation process;
(3) blending the granules obtained in the step (2) with extragranular raw materials;
(4) compressing the blend from the step (3) into a tablet; and
(5) film coating the tablet from the step (4).

21. The process of claim 20, comprising the steps of:
(1) blending raw materials with crystalline apixaban particles to form a mix;
(2) adding intragranular portions of a binder, a disintegrant and at least one filler to the mix from the step (1) to form a blend:
(3) granulating the materials from the step (2) using a dry granulation process or a wet granulation process, wherein the dry granulation process comprises:
delumping an intragranular lubricant using a screen or mill; adding the intragranular lubricant to the blend from the step (2) and blending to form a lubricated blend;
compacting the lubricated blend to ribbons of density in the range of 1.1 to 1.2 g/cc and sizing the compacted ribbons using a roller compactor, and wherein the wet granulation process comprises:
wet granulating the blend from the step (2) using water to a target end point and, optionally, sizing the wet granules by passing through a screen or mill;
removing the water from the granulation by drying in a convection oven or fluid-bed dryer;
and sizing the dried granules by passing through a screen or mill;
(4) blending the granules obtained in the step (3) and an extragranular disintegrant in a blender;

(5) delumping an extragranular lubricant using a screen or mill and blending with granules from the step (4);

(6) compressing the blend from the step (5) into a tablet; and

(7) film coating the tablet from the step (6).

22. The process of claim 20 or 21, wherein the dry granulation process is used.

23. A tablet comprising about 2.5 mg to about 5 mg of apixaban and a pharmaceutically acceptable diluent or carrier, which is prepared by a process comprising:
blending raw materials comprising crystalline apixaban particles having a D90 equal to or less than about 89 μm as measured by laser light scattering; and
granulating,
wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the tablet dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate.

24. The tablet as defined in claim 23, wherein the process comprises the steps of:

(1) blending raw materials comprising crystalline apixaban particles prior to granulation;

(2) granulating the raw materials from the step (1) using a dry granulation process;

(3) blending the granules obtained in the step (2) with extragranular raw materials;

(4) compressing the blend from the step (3) into a tablet; and

(5) film coating the tablet from the step (4).

25. The tablet as defined in claim 24, wherein the process comprises the steps of:

(1) blending raw materials with crystalline apixaban particles to form a mix;

(2) adding intragranular portions of a binder, a disintegrant and at least one filler to the mix from the step (1) to form a blend:

(3) granulating the materials from the step (2) using a dry granulation process, which comprises:

delumping an intragranular lubricant using a screen or mill; adding the intragranular lubricant to the blend from the step (2) and blending to form a lubricated blend;

compacting the lubricated blend to ribbons of density in the range of 1.1 to 1.2 g/cc and sizing the compacted ribbons using a roller compactor,

(4) blending the granules obtained in the step (3) and an extragranular disintegrant in a

blender;

(5) delumping an extragranular lubricant using a screen or mill and blending with granules from the step (4);

(6) compressing the blend from the step (5) into a tablet; and

(7) film coating the tablet from the step (6).

26. The tablet as defined in any one of claims 23 to 25, wherein the crystalline apixaban particles have a D90 equal to or less than 85 μm as measured by laser light scattering.

27. The tablet as defined in any one of claims 23 to 26, wherein the crystalline apixaban particles have a D90 equal to or less than 50 μmas measured by laser light scattering.

28. The tablet as defined in any one of claims 23 to 27, wherein the crystalline apixaban particles have a D90 equal to or less than 25 μm as measured by laser light scattering.

29. The tablet as defined in any one of claims 23 to 28, wherein the crystalline apixaban particles comprise Form N-1 of apixaban.

30. The tablet as defined in any one of claims 23 to 29, wherein the tablet contains 2.5 mg of apixaban.

31. The tablet as defined in any one of claims 23 to 29, wherein the tablet contains 5 mg of apixaban.

32. The tablet as defined in any one of claims 23 to 31, wherein:

the intragranular ingredients are apixaban, anhydrous lactose, microcrystalline cellulose, sodium croscarmellose, magnesium stearate, and sodium lauryl sulfate; and

the extragranular ingredients are sodium croscannellose and magnesium stearate.

33. A tablet comprising from about 2.5 mg to about 5 mg of apixaban and a pharmaceutically acceptable diluent or carrier,

wherein the tablet is prepared using crystalline apixaban particles having a D90 equal to or less than about 89 μm as a raw material as measured by laser light scattering, and

wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the tablet dissolves within 30

minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate.

34. The tablet as defined in claim 33, comprising 2.5 mg of apixaban.

35. The tablet as defined in claim 33, comprising 5 mg of apixaban.

36. A capsule comprising from about 2.5 mg to about 5 mg of apixaban and a pharmaceutically acceptable diluent or carrier,

wherein the capsule is prepared using crystalline apixaban particles having a D90 equal to or less than about 89 μm as a raw material as measured by laser light scattering, and

wherein, as measured using a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 mL of a dissolution medium at 37 °C, at least 77 wt% of apixaban in the capsule dissolves within 30 minutes in the dissolution medium, and the dissolution medium is 0.05 M sodium phosphate at a pH 6.8 containing 0.05% sodium lauryl sulfate.

37. The capsule as defined in claim 36, comprising 2.5 mg of apixaban.

38. The capsule as defined in claim 36, comprising 5 mg of apixaban.

39. The composition as defined in any one of claims 1 to 18 for use in treating or preventing a thromboembolic disorder.

40. The composition as defined in claim 39, wherein the thromboembolic disorder is selected from the group consisting of deep vein thrombosis, stroke, and pulmonary embolism.

41. The tablet as defined in any one of claims 23 to 35 for use in treating or preventing a thromboembolic disorder.

42. The tablet as defined in claim 41 wherein the thromboembolic disorder is selected from the group consisting of deep vein thrombosis, stroke, and pulmonary embolism.

43. Use of apixaban in a composition as defined in any one of claims 1 to 18 or in a tablet as defined in any one of claims 23 to 35 in the manufacture of a medicament for the treatment or prevention of a venous thromboembolic event.

44. Use of apixaban in a composition as defined in any one of claims 1 to 18 or in a tablet as defined in any one of claims 23 to 35 in the manufacture of a medicament for the prevention of stroke.

45. Use of apixaban in a composition as defined in any one of claims 1 to 18 or in a tablet as defined in any one of claims 23 to 35 in the manufacture of a medicament for the treatment or prevention of deep vein thrombosis or pulmonary embolism.

46. The use as defined in claim 43, wherein the venous thromboembolic event is selected from the group consisting of deep vein thrombosis, stroke, and pulmonary embolism.