FORMULATIONS OF APREMILAST

BACKGROUND

[0001] Apremilast is a phosphodiesterase subtype IV ("PDE4") inhibitor and has been approved worldwide for the treatment of various diseases associated with inflammation. For example, in the United States apremilast is approved for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or system therapy, for the treatment of adult patients with active psoriatic arthritis, and for the treatment of adult patients with oral ulcers associated with Behcet's Disease. Apremilast was the first, and remains the only, orally administered PDE4 inhibitor approved for the treatment of these inflammatory diseases. The recommended dosage for adult patients with active PsA and psoriasis is 30 mg twice daily (BID) orally, following a 5-day titration that is intended to reduce the gastrointestinal (GI) symptoms associated with initial therapy.

[0002] A goal in developing a drug is to provide dosage forms which make it possible to maintain a certain amount or concentration of drug in a subject's body that is clinically or therapeutically relevant. In some cases, this may not be achieved by traditional rapidly disintegrating tablets, as these tablets release the active ingredient contained therein all at once.

[0003] In view of the foregoing, there remains a need for oral dosage forms of apremilast that provide clinically desirable drug exposure.

SUMMARY

[0004] In one aspect, the present disclosure provides oral dosage forms comprising a core tablet comprising (i) a drug layer comprising apremilast and hypromellose acetate succinate (HPMCAS) in an amorphous solid dispersion; and (ii) a swellable layer comprising one or more swellable polymers; and a coating layer disposed on the core tablet, wherein the oral dosage form surface comprises at least one drug release orifice.

[0005] In another aspect, the present disclosure further provides oral dosage forms comprising a core tablet comprising (i) a drug layer comprising 8-11 wt% apremilast based upon total core tablet weight, 8-11 wt% hypromellose acetate succinate (HPMCAS) based upon total core tablet weight, 2-7 wt% mannitol based upon total core tablet weight, 40-45 wt% polyethylene oxide based upon total core tablet weight, 0.1-0.5 wt% magnesium stearate based upon total core tablet weight, and 0.1-0.5 wt% colloidal silicon dioxide based upon total core tablet weight, wherein the apremilast and HPMCAS are in a solid dispersion; (ii) a swellable layer comprising 18-25 wt% polyethylene oxide based upon total core tablet weight, 7-10 wt% microcrystalline cellulose based upon total core tablet weight, 1.5-3.5 wt.% sodium chloride based upon total core tablet weight, 0.01-0.2 wt% iron oxide based upon total core tablet weight, and 0.05-0.3 wt% magnesium stearate based upon total core tablet weight; and a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprising at least one drug release orifice.

[0005a] In another aspect, the present disclosure refers to an oral dosage form comprising (a) a core tablet comprising (i) a drug layer comprising 9-15 wt.% apremilast based upon total core tablet weight, 10-15 wt% hypromellose acetate succinate (HPMCAS) based upon total core tablet weight, 0-27 wt% mannitol based upon total core tablet weight, 30-40 wt% polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a mixture thereof based upon total core tablet weight, 2-8 wt% sodium chloride based upon total core tablet weight, 0.1-0.5 wt% magnesium stearate based upon total core tablet weight, and 0.1-0.5 wt% colloidal silicon dioxide

based upon total core tablet weight, wherein the apremilast and HPMCAS are in a solid dispersion; (ii) a swellable layer comprising 15-25 wt% polyethylene oxide with molecular weight of 5,000,000 Da based upon total core tablet weight, 5-10.0 wt% microcrystalline cellulose based upon total core tablet weight, 2-4 wt% sodium chloride based upon total core tablet weight, 0.01-0.1 wt% iron oxide based upon total core tablet weight, and 0.05-0.3 wt% magnesium stearate based upon total core tablet weight; and (b) a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

[0006] The disclosure also provides oral dosage forms comprising a core tablet comprising (i) a drug layer comprising 10-15 wt.% apremilast based upon total core tablet weight, 10-15 wt% hypromellose acetate

succinate (HPMCAS) based upon total core tablet weight, 30-40 wt% polyethylene oxide based upon total core tablet weight, 2-8 wt% sodium chloride based upon total core tablet weight, 0.1-0.5 wt% magnesium stearate based upon total core tablet weight, and 0.1-0.5 wt% colloidal silicon dioxide based upon total core tablet weight, wherein the apremilast and HPMCAS are in a solid dispersion; (ii) a swellable layer comprising 18-25 wt% polyethylene oxide based upon total core tablet weight, 7.5-10.0 wt% microcrystalline cellulose based upon total core tablet weight, 2-4 wt% sodium chloride based upon total core tablet weight, 0.01-0.1 wt% iron oxide based upon total core tablet weight, and 0.05-0.3 wt% magnesium stearate based upon total core tablet weight; and a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprising at least one drug release orifice.

[0006a] In yet another aspect, the present disclosure refers to the use of an oral dosage form as described herein in the manufacture of a medicament for treating a disease or disorder ameliorated by inhibiting PDE4, wherein the oral dosage form is to be administered once daily under fed conditions.

[0006b] In another aspect, the present disclosure refers to the oral dosage form as described herein for use in therapy.

BRIEF DESCRIPTION OF THE FIGURES

[0007] Figure 1 shows dissolution profiles of Tablets 6-10.

[0008] Figure 2 shows dissolution profiles of Tablets 1-5.

[0009] Figure 3 shows dissolution profiles of tablet core 5 uncoated or with a CA or PEG coating.

[0010] Figure 4 shows dissolution profiles of Tablets 10-12.

[0011] Figure 5 shows Mean (± SD) Apremilast Plasma Concentrations – Time Profiles.

[0012] Figure 6 shows apremilast plasma concentrations over 24 hours of 75 mg Tablet 21 once a day (open circles), compared to a 30 mg immediate release formulation twice a day (filled circles) and 75 mg gastrorentive (GR) tablet once a day (filled diamonds).

[0013] Figure 7 shows apremilast plasma concentrations over 5 days of 75 mg Tablet 21 once a day (open circles), compared to a 30 mg immediate release formulation twice a day (filled circles) and 75 mg gastrorentive (GR) tablet once a day (filled diamonds)..

[0014] Figure 8 shows the dissolution of Core Tablet Compositions 7-1 through 7-6.

[0015] Figure 9 shows the dissolution of Core Tablet Compositions 7-7 through 7-12.

[0016] Figure 10A shows decreased dissolution of Core Tablet Composition 7-8 after various storage conditions.

[0017] Figure 10B shows increased crystallinity in Core Tablet Composition 7-8 after various storage conditions.

[0018] Figure 11A shows dissolution of Core Tablet Compositions 7-12 after various storage conditions.

[0019] Figure 11B shows comparison of crystallinity in Core Tablet Composition 7-8 and 7-12 after various storage conditions.

DETAILED DESCRIPTION

[0020] Provided herein are oral dosage forms suitable for providing once-a-day (QD) dosing of apremilast. In some embodiments, the disclosed oral dosage forms are administered under fed conditions.

What is Claimed:

1. An oral dosage form comprising:

    a. a core tablet comprising

    (i) a drug layer comprising apremilast and hypromellose acetate succinate (HPMCAS) in an amorphous solid dispersion; and

    (ii) a swellable layer comprising one or more swellable polymers; and

    b. a coating layer disposed on the core tablet,

wherein the oral dosage form surface comprises at least one drug release orifice.

2. The oral dosage form of claim 1, wherein the apremilast is present in an amount of 6-15 wt% of the core tablet.

3. The oral dosage form of claim 1 or 2, wherein the solid dispersion is spray-dried.

4. The oral dosage form of any one of claims 1-3, wherein the HPMCAS is present in an amount of 6-15 wt% of the core tablet.

5. The oral dosage form of any one of claims 1-4, wherein apremilast and HPMCAS are present in a weight ratio of 45:55 to 55:45 in the core tablet.

6. The oral dosage form of claim 5, wherein apremilast and HPMCAS are present in a weight ratio of 48:52 to 52:48.

7. The oral dosage form of claim 5, wherein apremilast and HPMCAS are present in a weight ratio of 50:50.

8. The oral dosage form of any one of claims 1-7, wherein the drug layer further comprises one or more of a water soluble polymer, a diluent, an osmotic agent, and a lubricant.

9. The oral dosage form of claim 8, wherein the water soluble polymer is present in an amount of 30-55 wt% of the core tablet.

10. The oral dosage form of claim 8 or 9, wherein the water soluble polymer comprises polyethylene oxide.

11. The oral dosage form of claim 10, wherein the polyethylene oxide has an average molecular weight of 200,000-600,000 Da.

12. The oral dosage form of claim 11, wherein the drug layer comprises polyethylene oxide having an average molecular weight of 200,000 Da.

13. The oral dosage form of claim 11, wherein the drug layer comprises polyethylene oxide having an average molecular weight of 300,000 Da.

14. The oral dosage form of claim 11, wherein the drug layer comprises polyethylene oxide having an average molecular weight of 600,000 Da.

15. The oral dosage form of any one of claims 8-14, wherein the water soluble polymer and apremilast are present in a weight ratio of 2 to 6:1, in the drug layer.

16. The oral dosage form of any one of claims 8-15, wherein the diluent comprises mannitol.

17. The oral dosage form of any one of claims 8-16, wherein the diluent is present in an amount of 2-7 wt% of the core tablet.

18. The oral dosage form of any one of claims 8-17, wherein the drug layer comprises intragranular diluent and extragranular diluent.

19. The oral dosage form of any one of claim 8-18, wherein the osmotic agent is present in the drug layer in an amount of 3-8 wt% of the core tablet.

20. The oral dosage form of any one of claims 8-19, wherein the osmotic agent in the drug layer comprises sodium chloride.

21. The oral dosage form of any one of claims 8-20, wherein the lubricant comprises magnesium stearate.

22. The oral dosage form of any one of claims 8-21, wherein the lubricant of the drug layer is present in an amount of 0.05-0.5 wt% of the core tablet.

23. The oral dosage form of any one of claims 1-22, wherein the drug layer further comprises extragranular glidant, extragranular lubricant, or both.

24. The oral dosage form of claim 23, wherein the extragranular glidant comprises silicon dioxide.

25. The oral dosage form of claim 23 or 24, wherein the extragranular lubricant comprises magnesium stearate.

26. The oral dosage form of any one of claims 1-25, wherein the drug layer and swellable layer are present in a weight ratio of 2:1 in the core tablet.

27. The oral dosage form of any one claims 1-26, wherein the swellable polymer comprises polyethylene oxide.

28. The oral dosage form of claim 27, wherein the polyethylene oxide has an average molecular weight of 5,000,000 Da.

29. The oral dosage form of any one of claims 1-28, wherein the swellable layer further comprises one or more of an osmotic agent, a diluent, a lubricant, and a colorant.

30. The oral dosage form of claim 29, wherein the osmotic agent of the swellable layer comprises sodium chloride.

31. The oral dosage form of claim 29 or 30, wherein the osmotic agent in the swellable layer is present in an amount of 2.5-3.5 wt% of the core tablet.

32. The oral dosage form of any one of claims 29-31, wherein the diluent of the swellable layer comprises microcrystalline cellulose.

33. The oral dosage form of any one of claims 29-32, wherein the diluent in the swellable layer is present in an amount of 7-10 wt% of the core tablet.

34. The oral dosage form of any one of claims 29-33, wherein the lubricant of the swellable layer comprises magnesium stearate.

35. The oral dosage form of any one of claims 29-34, where the lubricant of the swellable layer is present in an amount of 0.05-0.5 wt% of the core tablet.

36. The oral dosage form of any one of claims 29-35, wherein the colorant comprises iron oxide red.

37. The oral dosage form of any one of claims 29-36, where the colorant is present in an amount of 0.05-0.5 wt% of the core tablet.

38. The oral dosage form of any one of claims 1-37, wherein the coating comprises cellulose acetate and polyethylene glycol.

39. The oral dosage form of claim 38, wherein the cellulose acetate and polyethylene glycol are present in a weight ratio 3.5 to 4.5:1 in the coating.

40. The oral dosage form of any one of claims 1-39, wherein the coating comprises 6.5-8.5 wt% of the total weight of the oral dosage form.

41. The oral dosage form of claim 40, wherein the coating comprises 7.5 wt% of the total weight of the oral dosage form.

42. The oral dosage form of any one of claims 1-41, further comprising a sub-coat layer between the core tablet and the coating layer.

43. The oral dosage form of claim 42, wherein the sub-coat layer comprises hydroxypropyl methylcellulose.

44. The oral dosage form of claim 42 or 43, wherein the sub-coat layer is present in an amount of 2-4 wt% of the oral dosage form.

45. The oral dosage form of claim 44, wherein the sub-coat layer is present in an amount of 2.3 wt% of the oral dosage form.

46. The oral dosage form of claim 44, wherein the sub-coat layer is present in an amount of 3.4 wt% of the oral dosage form.

47. The oral dosage form of any one of claims 1-46, wherein the drug layer comprises an intragranular portion and an extragranular portion.

48. The oral dosage form of claim 47, wherein the extragranular portion comprises a lubricant and a glidant.

49. The oral dosage form of claim 48, wherein the extragranular portion further comprises a diluent.

50. The oral dosage form of claim 49, wherein the lubricant comprises magnesium stearate, the glidant comprises silicon dioxide, and the diluent comprises mannitol.

51. The oral dosage form of any one of claims 47-50, wherein the intragranular portion comprises apremilast, HPMCAS, polyethylene oxide, and mannitol, and an intragranular lubricant.

52. The oral dosage form of claim 51, wherein the intragranular lubricant comprises magnesium stearate.

53. The oral dosage form of any one of claims 49-52, wherein the mannitol is present in both the intragranular portion and the extragranular portion.

54. The oral dosage form of claim 53, comprising 55-57% of the total mannitol present is in the intragranular portion and 43-45% of the total mannitol present is in the extragranular portion.

55. The oral dose form of any one of claims 47-54, wherein the swellable layer further comprises a lubricant.

56. The oral dosage form of claim 55, wherein the lubricant of the swellable layer comprises magnesium stearate.

57. The oral dosage form of any one of claims 47-56, wherein the drug layer intragranular portion comprises sodium chloride.

58. The oral dosage form of any one of claims 47-57, further comprising a color coat layer in an amount of 3-5 wt% of the oral dosage form.

59. The oral dosage form of claim 58, wherein the color coat layer is present in an amount of 3.4 wt% of the oral dosage form.

60. An oral dosage form comprising:

a. a core tablet comprising

(i) a drug layer comprising 8-11 wt% apremilast based upon total core tablet weight, 8-11 wt% hypromellose acetate succinate (HPMCAS) based upon total core tablet weight, 2-7 wt% mannitol based upon total core tablet weight, 40-45 wt% polyethylene oxide with molecular weight of 200,000 Da based upon total core tablet weight, 0.1-0.5 wt% magnesium stearate based upon total core tablet weight, and 0.1-0.5 wt% colloidal silicon dioxide based upon total core tablet weight, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 18-25 wt% polyethylene oxide with molecular weight of 5,000,000 Da based upon total core tablet weight, 7-10 wt% microcrystalline cellulose based upon total core tablet weight, 1.5-3.5 wt.% sodium chloride based upon total core tablet weight, 0.01-0.2 wt% iron oxide based upon total core tablet weight, and 0.05-0.3 wt% magnesium stearate based upon total core tablet weight; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

61. The oral dosage form of claim 60 comprising:

a. a core tablet comprising

(i) a drug layer comprising 75 mg apremilast, 75 mg hypromellose acetate succinate (HPMCAS), 22.1 mg mannitol, 314.8 mg polyethylene oxide with molecular weight of 200,000 Da, 2.4 mg magnesium stearate, and 2.5 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 159.6 mg polyethylene oxide with molecular weight of 5,000,000 Da, 63.4 mg microcrystalline cellulose, 21.1 mg sodium chloride, 0.5 mg iron oxide, and 1.2 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

62. The oral dosage form of claim 60 comprising:

a. a core tablet comprising

(i) a drug layer comprising 55 mg apremilast, 55 mg hypromellose acetate succinate (HPMCAS), 16.2 mg mannitol, 230.9 mg polyethylene oxide with molecular weight of 200,000 Da, 1.7 mg magnesium stearate, and 1.8 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 117 mg polyethylene oxide with molecular weight of 5,000,000 Da, 46.5 mg microcrystalline cellulose, 15.5 mg sodium chloride, 0.4 mg iron oxide, and 0.9 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

63. The oral dosage form of claim 60 comprising:

a. a core tablet comprising

(i) a drug layer comprising 27.5 mg apremilast, 27.5 mg hypromellose acetate succinate (HPMCAS), 8.1 mg mannitol, 115.6 mg polyethylene oxide with molecular weight of 200,000 Da, 1.0 mg magnesium stearate, and 0.9 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 58.6 mg polyethylene oxide with molecular weight of 5,000,000 Da, 23.3 mg microcrystalline cellulose, 7.8 mg sodium chloride, 0.2 mg iron oxide, and 0.5 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

64. An oral dosage form comprising:

a. a core tablet comprising

(i) a drug layer comprising 9-15 wt.% apremilast based upon total core tablet weight, 10-15 wt% hypromellose acetate succinate (HPMCAS) based upon total core tablet weight, 0-27 wt% mannitol based upon total core tablet weight, 30-40 wt% polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a mixture thereof based upon total core tablet weight, 2-8 wt% sodium chloride based upon total core tablet weight, 0.1-0.5 wt% magnesium

stearate based upon total core tablet weight, and 0.1-0.5 wt% colloidal silicon dioxide based upon total core tablet weight, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 15-25 wt% polyethylene oxide with molecular weight of 5,000,000 Da based upon total core tablet weight, 5-10.0 wt% microcrystalline cellulose based upon total core tablet weight, 2-4 wt% sodium chloride based upon total core tablet weight, 0.01-0.1 wt% iron oxide based upon total core tablet weight, and 0.05-0.3 wt% magnesium stearate based upon total core tablet weight; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

65. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 100 mg apremilast, 100 mg hypromellose acetate succinate (HPMCAS), 301.4 mg polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a mixture thereof, 26.7 mg sodium chloride, 2.6 mg magnesium stearate, and 2.7 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 173.1 mg polyethylene oxide with molecular weight of 5,000,000 Da, 68.8 mg microcrystalline cellulose, 22.9 mg sodium chloride, 0.5 mg iron oxide, and 1.3 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

66. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 100 mg apremilast, 100 mg hypromellose acetate succinate (HPMCAS), 274.6 mg polyethylene oxide with molecular weight of 300,000 Da, 53.3 sodium chloride, 2.6 mg magnesium stearate, and 2.7 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 173.1 mg polyethylene oxide with molecular weight of 5,000,000 Da, 68.8 mg microcrystalline cellulose, 22.9 mg sodium chloride, 0.5 mg iron oxide, and 1.3 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

67. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 75 mg apremilast, 75 mg hypromellose acetate succinate (HPMCAS), 226.0 mg polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a

mixture thereof, 20.0 mg sodium chloride, 2.0 mg magnesium stearate, and 2.0 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 129.8 mg polyethylene oxide with molecular weight of 5,000,000 Da, 51.6mg microcrystalline cellulose, 17.2 mg sodium chloride, 0.4 mg iron oxide, and 1.0 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

68. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 75 mg apremilast, 75 mg hypromellose acetate succinate (HPMCAS), 206.0 mg polyethylene oxide with molecular weight of 300,000 Da, 40.0 mg sodium chloride, 2.0 mg magnesium stearate, and 2.0 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 129.8 mg polyethylene oxide with molecular weight of 5,000,000 Da, 51.6 mg microcrystalline cellulose, 17.2 mg sodium chloride, 0.4 mg iron oxide, and 1.0 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

69. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 55 mg apremilast, 55 mg hypromellose acetate succinate (HPMCAS), 165.7 mg polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a mixture thereof, 14.7 mg sodium chloride, 1.4 mg magnesium stearate, and 1.5 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 95.2 mg polyethylene oxide with molecular weight of 5,000,000 Da, 37.8 mg microcrystalline cellulose, 12.6 mg sodium chloride, 0.3 mg iron oxide, and 0.7 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

70. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 55 mg apremilast, 55 mg hypromellose acetate succinate (HPMCAS), 151.1 mg polyethylene oxide with molecular weight of 300,000 Da, 29.3 mg sodium chloride, 1.4 mg magnesium stearate, and 1.5 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 95.2 mg polyethylene oxide with molecular weight of 5,000,000 Da, 37.8 mg microcrystalline cellulose, 12.6 mg sodium chloride, 0.3 mg iron oxide, and 0.7 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

71. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 27.5 mg apremilast, 27.5 mg hypromellose acetate succinate (HPMCAS), 82.9 mg polyethylene oxide with molecular weight of 200,000 to 300,000 Da or a mixture thereof, 7.3 mg sodium chloride, 0.8 mg magnesium stearate, and 0.7 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 47.6 mg polyethylene oxide with molecular weight of 5,000,000 Da, 18.9 mg microcrystalline cellulose, 6.3 mg sodium chloride, 0.1 mg iron oxide, and 0.4 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

72. The oral dosage form of claim 64 comprising:

a. a core tablet comprising

(i) a drug layer comprising 27.5 mg apremilast, 27.5 mg hypromellose acetate succinate (HPMCAS), 75.5 mg polyethylene oxide with molecular weight of 300,000 Da, 14.7 mg sodium chloride, 0.4 mg magnesium stearate, and 0.7 mg colloidal silicon dioxide, wherein the apremilast and HPMCAS are in a solid dispersion;

(ii) a swellable layer comprising 47.6 mg polyethylene oxide with molecular weight of 5,000,000 Da, 18.9 mg microcrystalline cellulose, 6.3 mg sodium chloride, 0.1 mg iron oxide, and 0.4 mg magnesium stearate; and

b. a coating layer disposed on the core tablet and comprising cellulose acetate and polyethylene glycol; wherein the oral dosage form surface comprises at least one drug release orifice.

73. Use of an oral dosage form of any one of claims 1-72 in the manufacture of a medicament for treating a disease or disorder ameliorated by inhibiting PDE4, wherein the oral dosage form is to be administered once daily under fed conditions.

74. The use of claim 73, wherein the disease or disorder is psoriasis, psoriatic arthritis, or Behcet's disease.

75. The use of claim 73, wherein the disease or disorder is colitis, inflammatory bowel disease, or hidradenitis suppurativa.

76. The use of claim 75, wherein the disease or disorder is colitis.

77. The use of claim 76, wherein the colitis is ulcerative colitis.

78. The use of claim 75, wherein the disease or disorder is inflammatory bowel disease.

79. The use of claim 75, wherein the disease or disorder is hidradenitis suppurativa.

80. The oral dosage form of any one of claims 1-72 for use in therapy.