CLAIMS

1. Crystalline anhydrous polymorph A1 of Compound A characterized by the following crystal data,

$C_{15}H_{20}N_6O_6$;

Mr = 380.37;

Monoclinic crystal system;

$P2_1$ space group;

a = 5.546(2) Å;

b = 7.107(2) Å;

c = 21.929(9) Å;

V = 858.8(5) $Å^3$, and

Z = 2.

2. Crystalline anhydrous polymorph A1 of Compound A characterized by substantially equivalent peaks at a reflection angle 2-theta as shown in Table 3.

3. A crystalline anhydrous polymorph according to Claim 1 or Claim 2 that is at least about 75% free of other forms.

4. A crystalline anhydrous polymorph according to any of Claims 1 to 3 that is at least about 80% free of other forms.

5. A crystalline anhydrous polymorph according to any of Claims 1 to 4 that is at least about 90% free of other forms.

6. A crystalline anhydrous polymorph according to any of Claims 1 to 5 that is at least about 95% free of other forms.

7. A crystalline anhydrous polymorph according to any of Claims 1 to 6 that is at least about 99% free of other forms.

8. A crystalline anhydrous polymorph according to any of Claims 1 to 7 that is 100% free of other forms.

9. A method of obtaining a crystalline anhydrous polymorph according to any of Claims 1 to 8, the method comprising the steps of preparing compound A as API as defined herein and recrystallizing at least twice from ethanol.

10. A method of obtaining a crystalline anhydrous polymorph according to any of Claims 1 to 8, the method comprising the steps of taking Compound A and recrystallizing from isopropanol, ethyl acetate, or isopropyl acetate.

11. A method of obtaining a crystalline anhydrous polymorph according to any of Claims 1 to 8, the method comprising the steps of taking Compound A and recrystallizing from 1,4 dioxane, 2-methoxy ethanol, 3-methyl-2-butanone, methylethyl ketone, or 1,2-dimethoxyethane.

12. A pharmaceutical composition comprising polymorph A1 as defined above and further comprising one or more pharmaceutically acceptable ingredients selected from the group consisting of carriers, excipients, diluents, additives, fillers, surfactants, binders, antimicrobial preservatives, viscosity enhancing agents, and buffers.

13. A pharmaceutical composition comprising polymorph A1 as defined in Claim 12 that is formulated for ophthalmic administration.

14. A polymorph A1 as defined in any of Claims 1 to 8 for use in a method of treating a subject in need of a selective adenosine A_1 agonist, the method comprising administering to a subject in need thereof a therapeutically effective amount of the polymorph A1.

15. A polymorph A1 as defined in any of Claims 1 to 8 for use in a method of reducing intraocular pressure in a subject, the method comprising topically administering to an eye of a subject in need thereof a therapeutically effective amount of a pharmaceutical composition according to Claim 13.

16. Crystalline anhydrous polymorph A2 characterized by the following crystal data,

$C_{15}H_{20}N_6O_6$;

Mr = 380.37;

Orthorhombic crystal system;

$P2_12_12_1$ space group;

a = 5.51796(17) Å;

b = 7.14615(29) Å;

c = 42.9738(29) Å and

V = 1694.55(14) $Å^3$;

in which the crystalline polymorph A2 is substantially free of other solid forms of Compound A.

17. Crystalline anhydrous polymorph A2 of Compound A characterized by substantially equivalent peaks at a reflection angle 2-theta as shown in Table 5; in which the crystalline polymorph A2 is substantially free of other solid forms of Compound A.

18. A crystalline anhydrous polymorph according to Claim 16 or Claim 17 that is at least about 75% free of other solid forms of Compound A.

19. A crystalline anhydrous polymorph according to any of Claims 16 to 18 that is at least about 80% free of other solid forms of Compound A.

20. A crystalline anhydrous polymorph according to any of Claims 16 to 19 that is at least about 90% free of other solid forms of Compound A.

21. A crystalline anhydrous polymorph according to any of Claims 16 to 20 that is at least about 95% free of other solid forms of Compound A.

22. A crystalline anhydrous polymorph according to any of Claims 16 to 21 that is at least about 99% free of other solid forms of Compound A.

23. A crystalline anhydrous polymorph according to any of Claims 16 to 22 that is 100% free of other solid forms of compound A.

24. A pharmaceutical composition comprising a crystalline anhydrous polymorph according to any of Claims 16 to 22 and further comprising one or more pharmaceutically acceptable ingredients selected from the group consisting of carriers, excipients, diluents, additives, fillers, surfactants, binders, antimicrobial preservatives, viscosity enhancing agents, and buffers.

25. A pharmaceutical composition according to Claim 24 that is formulated for ophthalmic administration.

26. A pharmaceutical composition according to Claim 24 that comprises:

Ingredient	%, W/V
Compound A	0.152 – 0.76
Sodium CMC	0.7
Benzalkonium Chloride	0.01
Polysorbate 80	0.3
Citric Acid Monohydrate	0.152 (7mM)
NaOH/HCl	pH 5.1 ±0.1
NaCl	q.s. to 270-330 mOsm; and
Purified Water	q.s. to 100.00.

27. A polymorph A2 as defined in any of Claims 16 to 22 for use in a method of treating a subject in need of a selective adenosine A_1 agonist, the method comprising administering to a subject in need thereof a therapeutically effective amount of the polymorph A2.

28. A polymorph A2 as defined in any of Claims 16 to 22 for use in a method of reducing intraocular pressure in a subject, the method comprising topically administering to an eye of a subject in need thereof a therapeutically effective amount of a pharmaceutical composition according to Claim 25.

29. A method of obtaining the polymorph A2, the method comprising the steps of suspending Compound A in an aqueous liquid vehicle and heating to about 40 degrees for at least 9 hours.

30. A method according to Claim 29 in which the Compound A is micronized and then added to the liquid vehicle.

31. A method according to any of Claims 29 to 30 in which the Compound A is micronized into particle sizes less than 50 microns.

32. A method according to any of Claims 29 to 31 in which the step of heating to about 40 degrees C continues for at least 15 hours.

33. A method according to any of Claims 29 to 32 in which the liquid vehicle is adapted to provide an aqueous suspension of Compound A.

34. A method according to any of Claims 33 in which the liquid vehicle includes a surfactant and a preservative.

35. A method according to Claim 34 in which the surfactant is selected from polysorbate 80, polysorbate 60, polysorbate 40, polysorbate 20, polyoxyl 40 stearate, poloxamers, tyloxapol, POE 35 and castor oil.

36. A method according to Claim 34 or Claim 35 in which the preservative is selected from a quaternary ammonium salt, benzalkonium chloride, cetrimide, chlorobutanol, sorbic acid and boric acid.

37. Crystalline anhydrous polymorph form A1 of Compound A characterized by a PXRD spectra having peaks at about 17.5, 20.5, 21.2, 22.7, 24.8, 33.2 and 42.1 + 0.2 degrees 2 theta.

38. Crystalline anhydrous polymorph form A2 of Compound A characterized by PXRD spectra having peaks at about 16.9, 18.1, 19.1, 20.8, 21.3, 22.0, 22.8, 23.8, 24.9, 25.0, 29.1, 29.8, 34.2 and 35.8 + 0.2 degrees 2 theta.

CLAIMS

1. Crystalline anhydrous polymorph A1 of Compound A characterized by the following crystal data,

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$P2_1$ space group;

a = 5.546(2) Å;

b = 7.107(2) Å;

c = 21.929(9) Å;

V = 858.8(5) $Å^3$, and

Z = 2,

in which the crystalline anhydrous polymorph is at least about 75% free of other forms of Compound A.

2. Crystalline anhydrous polymorph A1 of Compound A characterized by substantially equivalent peaks at a reflection angle 2-theta as shown in Table 3.

3. A crystalline anhydrous polymorph according to Claim 1 or 2 that is at least about 80% free of other forms.

4. A crystalline anhydrous polymorph according to Claim 1, 2 or 3 that is at least about 90% free of other forms.

5. A crystalline anhydrous polymorph according to any preceding claim that is at least about 95% free of other forms.

6. A crystalline anhydrous polymorph according to any preceding claim that is at least about 99% free of other forms.

7. A crystalline anhydrous polymorph according to any preceding claim that is 100% free of other forms.

8. A method of obtaining a crystalline anhydrous polymorph according to any preceding claim, the method comprising the steps of preparing compound A as API as defined herein and recrystallizing at least twice from ethanol.

9. A method of obtaining a crystalline anhydrous polymorph according to any of Claims 1 to 7, the method comprising the steps of taking Compound A and recrystallizing from isopropanol, ethyl acetate, or isopropyl acetate.

10. A method of obtaining a crystalline anhydrous polymorph according to any of Claims 1 to 7, the method comprising the steps of taking Compound A and recrystallizing from 1,4 dioxane, 2-methoxy ethanol, 3-methyl-2-butanone, methylethyl ketone, or 1,2-dimethoxyethane.

11. A pharmaceutical composition comprising polymorph A1 as defined above and further comprising one or more pharmaceutically acceptable ingredients selected from the group consisting of carriers, excipients, diluents, additives, fillers, surfactants, binders, antimicrobial preservatives, viscosity enhancing agents, and buffers.

12. A pharmaceutical composition comprising polymorph A1 as defined in Claim 11 that is formulated for ophthalmic administration.

13. A polymorph A1 as defined in any of Claims 1 to 7 for use in a method of treating a subject in need of a selective adenosine A_1 agonist, the method comprising administering to a subject in need thereof a therapeutically effective amount of the polymorph A1.

14. A polymorph A1 as defined in any of Claims 1 to 7 for use in a method of reducing intraocular pressure in a subject, the method comprising topically administering to an eye of a subject in need thereof a therapeutically effective amount of a pharmaceutical composition according to Claim 13.

15. Crystalline anhydrous polymorph A2 characterized by the following crystal data,

$C_{15}H_{20}N_6O_6$;

Mr = 380.37;

Orthorhombic crystal system;

$P2_12_12_1$ space group;

a = 5.51796(17) Å;

b = 7.14615(29) Å;

c = 42.9738(29) Å and

V = 1694.55(14) $Å^3$;

in which the crystalline polymorph A2 is substantially free of other solid forms of Compound A.

16. Crystalline anhydrous polymorph A2 of Compound A characterized by substantially equivalent peaks at a reflection angle 2-theta as shown in Table 5; in which the crystalline polymorph A2 is substantially free of other solid forms of Compound A.

17. A crystalline anhydrous polymorph according to Claim 15 or 16 that is at least about 75% free of other solid forms of Compound A.

18. A crystalline anhydrous polymorph according to Claim 15, 16 or 17 that is at least about 80% free of other solid forms of Compound A.

19. A crystalline anhydrous polymorph according to any of Claims 15 to 18 that is at least about 90% free of other solid forms of Compound A.

20. A crystalline anhydrous polymorph according to any of Claims 15 to 19 that is at least about 95% free of other solid forms of Compound A.

21. A crystalline anhydrous polymorph according to any of Claims 15 to 20 that is at least about 99% free of other solid forms of Compound A.

22. A crystalline anhydrous polymorph according to any of Claims 15 to 21 that is 100% free of other solid forms of compound A.

23. A pharmaceutical composition comprising a crystalline anhydrous polymorph according to any of Claims 15 to 21 and further comprising one or more pharmaceutically acceptable ingredients selected from the group consisting of carriers, excipients, diluents, additives, fillers, surfactants, binders, antimicrobial preservatives, viscosity enhancing agents, and buffers.

24. A pharmaceutical composition according to Claim 23 that is formulated for ophthalmic administration.

25. A pharmaceutical composition according to Claim 23 that comprises:

Ingredient	%, W/V
Compound A	0.152 – 0.76
Sodium CMC	0.7
Benzalkonium Chloride	0.01
Polysorbate 80	0.3
Citric Acid Monohydrate	0.152 (7mM)
NaOH/HCl	pH 5.1 ±0.1
NaCl	q.s. to 270-330 mOsm; and
Purified Water	q.s. to 100.00.

26. A polymorph A2 as defined in any of Claims 15 to 21 for use in a method of treating a subject in need of a selective adenosine A_1 agonist, the method comprising administering to a subject in need thereof a therapeutically effective amount of the polymorph A2.

27. A polymorph A2 as defined in any of Claims 15 to 21 for use in a method of reducing intraocular pressure in a subject, the method comprising topically administering to an eye of a subject in need thereof a therapeutically effective amount of a pharmaceutical composition according to Claim 25.

28. A method of obtaining the polymorph A2, the method comprising the steps of suspending Compound A in an aqueous liquid vehicle and heating to about 40 degrees for at least 9 hours.

29. A method according to Claim 28 in which the Compound A is micronized and then added to the liquid vehicle.

30. A method according to Claim 28 or 29 in which the Compound A is micronized into particle sizes less than 50 microns.

31. A method according to Claim 28, 29 or 30 in which the step of heating to about 40 degrees C continues for at least 15 hours.

32. A method according to any of Claims 28 to 31 in which the liquid vehicle is adapted to provide an aqueous suspension of Compound A.

33. A method according to Claim 32 in which the liquid vehicle includes a surfactant and a preservative.

34. A method according to Claim 33 in which the surfactant is selected from polysorbate 80, polysorbate 60, polysorbate 40, polysorbate 20, polyoxyl 40 stearate, poloxamers, tyloxapol, POE 35 and castor oil.

35. A method according to Claim 33 or 34 in which the preservative is selected from a quaternary ammonium salt, benzalkonium chloride, cetrimide, chlorobutanol, sorbic acid and boric acid.

36. Crystalline anhydrous polymorph form A1 of Compound A characterized by a PXRD spectra having peaks at about 17.5, 20.5, 21.2, 22.7, 24.8, 33.2 and 42.1 + 0.2 degrees 2 theta.

37. Crystalline anhydrous polymorph form A2 of Compound A characterized by PXRD spectra having peaks at about 16.9, 18.1, 19.1, 20.8, 21.3, 22.0, 22.8, 23.8, 24.9, 25.0, 29.1, 29.8, 34.2 and 35.8 + 0.2 degrees 2 theta.