CLAIMS

1. A process for the preparation of a crystalline polymorph Form B of 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, wherein said Form B has an X-ray powder diffraction pattern measured using Cu Kα radiation with peaks at 2θ = about 9.6, 10.1, 11.4, 13.1, 13.9, 14.8, 15.4, 15.8, 17.0, 17.4, 18.5, 18.8, 19.7, 19.9, 20.5, 21.0, 21.9, 22.9, 23.6, 24.6 and 25.7°, the method comprising:

(a) dissolving 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, at a temperature of at least 40°C, in a non-aqueous solvent or mixture of non-aqueous solvents to obtain a solution, wherein the solvent or solvents contain less than about 5 wt% of water relative to the 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide starting material;

(b) cooling the solution;

(c) isolating the crystals;

(d) heating the resultant crystals to greater than 75°C for a period of greater than 1 minute to produce Form B 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide.

2. A process for the preparation of a crystalline polymorph Form B of 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, wherein said Form B has an X-ray powder diffraction pattern measured using Cu Kα radiation with peaks at 2θ = about 9.6, 10.1, 11.4, 13.1, 13.9, 14.8, 15.4, 15.8, 17.0, 17.4, 18.5, 18.8, 19.7, 19.9, 20.5, 21.0, 21.9, 22.9, 23.6, 24.6 and 25.7°, the method comprising:

(a) dissolving 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, at a temperature of at least 40°C, in a non-aqueous solvent or mixture of non-aqueous solvents to obtain a solution;

(b) cooling the solution;

wherein the temperature of process step (b) does not exceed 100°C;

(c) isolating the crystals;

(d) heating the resultant crystals to greater than 75°C for a period of greater than 1 minute to produce Form B 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide.

3. A process for the preparation of a crystalline polymorph Form B of 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, wherein said Form B has an X-ray powder diffraction pattern measured using Cu Kα radiation with peaks at 2θ = about 9.6, 10.1, 11.4, 13.1, 13.9, 14.8, 15.4, 15.8, 17.0, 17.4, 18.5, 18.8, 19.7, 19.9, 20.5, 21.0, 21.9, 22.9, 23.6, 24.6 and 25.7°, the method comprising:

(a) dissolving 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, at a temperature of 90°C or greater, preferably 100°C or greater, in a non-aqueous solvent or mixture of non-aqueous solvents to obtain a solution;

(b) optionally filtering the solution to substantially remove particles having a largest diameter greater than 100μm;

(c) cooling the solution to less than 100°C, preferably less than 90°C, but greater than 80°C;

(d) seeding the solution with Form B crystals of 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide;

(e) optionally cooling the solution further;

(f) optionally further seeding of the solution with Form B crystals of 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide;

(g) cooling the solution to less than 70°C

(h) isolating the crystals of Form B 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide.

4. The process according to any preceding claim, wherein the temperature of process step (a) is greater than 100°C.

5. The process according to claim 1, wherein the temperature of process step (d) is greater than 80°C, preferably greater than 85°C, preferably greater than 90°C, preferably greater than 100°C.

6. The process according to claim 1, 2 or 5, wherein the temperature of process step (d) is maintained for greater than 5 minutes, preferably greater than 15 minutes, preferably greater than 1 hour, preferably greater than 4 hours.

7. The process according to claim 1 or claim 2, wherein the cooling in step (b) is preferably at a cooling rate of about between 1 and 0.01 °C/min, preferably between 0.5 and 0.05 °C/min, preferably between 0.2 and 0.08 °C/min, preferably at about 0.1°C/min.

8. The process according to any preceding claim, wherein the nonaqueous solvent or mixture of non-aqueous solvents are selected from the group consisting of C_{1-6} alcohols, C_{4-10} cyclic ethers, C_{1-6} nitriles, C_{1-6} haloalkanes, C_{1-6} ketones, dialkylformamides, dialkyl sulfoxides, C_{3-10} aryls, C_{5-10} alkanes, C_{1-6} alkyl acetate, preferably in the substantial absence of water, optionally wherein the nonaqueous solvent or solvents are selected from the group consisting of methanol, ethanol, tetrahydrofuran, acetonitrile, methylene chloride, isopropyl alcohol, acetone, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), toluene, benzene, n-hexane, ethyl acetate, dichloromethane, chloroform and carbon tetrachloride, most preferably selected from ethanol, isopropyl alcohol and isobutanol.

9. The process according to claim 3, wherein the solvent or solvents in step (a) contain less than about 5 wt% of water relative to the 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide starting material; or
wherein the cooling step (g) is at a temperature of less than 50°C but greater than 0°C, preferably less than 30°C, preferably about 20°C, wherein this temperature is preferably maintained for at least 30 minutes, preferably 1 hour, preferably at least 2 hours, preferably at least 5 hours; or
wherein the solvent is removed in step (h) by drying between 40-120°C, preferably under vacuum, preferably 60-100°C, preferably under vacuum; or
wherein in step (g), the cool down rate is a maximum of 0.05 °C/min.

10. The process according to claim 3 or claim 9, wherein the temperature of the solution in step (a) is between 90°C and 200°C , preferably between 100°C and 180°C, preferably between 103°C and 125°C, preferably about 105°C.

11. The process according to claim 3, 9 or 10, wherein the filtration step (b) removes particles having a largest diameter of greater than 50μm, preferably greater

than 20μm, preferably greater than 10μm, preferably greater than 5μm, preferably greater than 1μm.

12. The process according to claim 3, 9, 10 or 11 wherein the cooling step (c) is a temperature of greater than 85°C, preferably about 88°C, and preferably this temperature is maintained for at least 1 hour, preferably at least 2 hours, preferably at least 5 hours.

13. The process according to any of claims 1 to 3, wherein during any cooling step, an anti-solvent is added, said anti-solvent preferably being selected from C_{1-6} ethers.

14. Form B 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide, wherein said Form B has an X-ray powder diffraction pattern measured using Cu Kα radiation with peaks at 2θ = about 9.6, 10.1, 11.4, 13.1, 13.9, 14.8, 15.4, 15.8, 17.0, 17.4, 18.5, 18.8, 19.7, 19.9, 20.5, 21.0, 21.9, 22.9, 23.6, 24.6 and 25.7°.

15. A pharmaceutical composition comprising Form B 3-[5-amino-4-(3-cyanobenzoyl)-pyrazol-1-yl]-N-cyclopropyl-4-methylbenzamide according to claim 14.