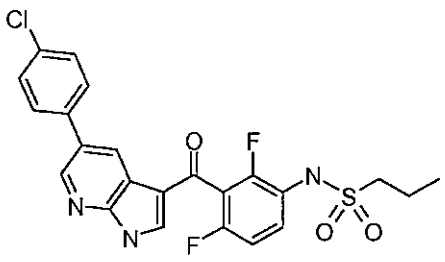
Claims

1. A solid form of the compound of formula 1,



(1),

wherein said solid form is selected from the group consisting of

a) a substantially amorphous form of compound 1 selected from form XVII, XVIII, XIX, XX, XXI, XXII, XXIII, XXIV, XXV, XXVI or combinations thereof, wherein the compound 1 is molecularly dispersed;

b) a solvate of form III, IV, V, VI, VII, IX, X, XI, XII, XIII, XIV or XV;

c) a polymorph of form VIII or XVI; and

d) the sulfuric acid-, hydrobromic acid- or hydrochloric acid salt of compound 1.

2. The solid form of claim 1, selected from a substantially amorphous form of compound 1 selected from form XVII, XVIII, XIX, XX, XXI, XXII, XXIII, XXIV, XXV, XXVI or combinations thereof, wherein compound 1 is molecularly dispersed within a polymer matrix.

3. The solid form (XVII) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 20.

4. The solid form (XVIII) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 21.

5. The solid form (XIX) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 22.

6. The solid form (XX) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 23.

7. The solid form (XXI) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 24.

8. The solid form (XXII) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 25.

9. The solid form (XXIII) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 26.

10. The solid form (XXIV) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 27.

11. The solid form (XXV) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 28.

12. The solid form (XXVI) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 29.

13. The solid form of any of claims 2-12, wherein the solid form is prepared by a spray dispersion process.

14. The solid form of any of claims 2-13, wherein the polymer is selected from hydroxypropyl methyl cellulose acetate succinate (HPMCAS), hydroxypropylmethyl cellulose, methacrylic acid copolymers, polyvinylpyrrolidone (povidone), 4-vinylpyrrolidone-vinyl acetate copolymer (copovidone) or copolymers of methacrylic acid and ethylacrylate (EUDRAGIT® L100-55).

15. A pharmaceutical composition comprising at least one solid form according to any of claims 2-14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, additives or excipients.

16. A method for treating a disease or condition in a mammal in need thereof, said method comprising: administering to said mammal an effective amount of a composition of claim 15.

17. The method of claim 16, wherein the disease or condition is melanoma, thyroid cancer or colon cancer.

18. The solid form of claim 1, selected from a solvate of form III, IV, V, VI, VII, IX, X, XI, XII, XIII, XIV or XV.

19. The solid form of claim 1, selected from a polymorph of form VIII or XVI.

20. The solid form of claim 1, selected from the sulfuric acid-, hydrobromic acid- or hydrochloric acid salt of compound 1.

21. A solid form (form III) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 9.5, 10.0, 13.0, 16.7, 18.7, 20.1, 21.0 and 25.6 degrees 2Theta (± 0.2 degrees 2Theta).

22. A solid form (form IV) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.5, 7.4, 11.0, 13.4, 14.8, 16.0, 16.7, 17.1, 17.9, 19.1, 19.5, 20.1, 20.5, 20.9, 21.2, 22.2, 23.0, 23.6, 24.2, 24.5 and 25.1 degrees 2Theta (± 0.2 degrees 2Theta).

23. A solid form (form V) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 12.7, 13.1, 14.3, 16.3, 19.0, 20.1, 22.4, 25.1, 27.1 and 28.9 degrees 2Theta (± 0.2 degrees 2Theta).

24. A solid form (form VI) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.8, 10.3, 11.4, 11.8, 15.1, 15.6, 16.1, 16.6, 18.6, 18.9, 19.2, 20.4, 21.0, 21.6, 22.8, 24.6, 25.1, 25.8, 26.1, 27.4 and 28.8 degrees 2Theta (± 0.2 degrees 2Theta).

25. A solid form (form VII) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.6, 9.4, 9.9, 13.1, 15.9, 16.2, 17.0, 18.1, 18.8, 19.9, 20.5, 20.7, 21.4, 21.8, 24.3, 24.9 and 25.3 degrees 2Theta (± 0.2 degrees 2Theta).

26. A solid form (form IX) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 9.5, 9.9, 13.0, 15.9, 16.4, 17.0, 17.9, 18.7, 19.9, 20.7, 21.7, 24.8 and 25.1 degrees 2Theta (± 0.2 degrees 2Theta).

27. A solid form (form X) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.4, 9.2, 10.8, 13.6, 14.9, 19.0, 20.2, 21.4, 22.4, 23.7, 25.5, 27.0 and 29.8 degrees 2Theta (± 0.2 degrees 2Theta).

28. A solid form (form XI) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 8.0, 12.1, 12.6, 13.4, 13.9, 14.8, 16.2, 17.6, 18.5, 19.2, 20.1, 21.0, 21.4, 21.7, 23.5, 25.3, 25.5, 26.6, 27.0 and 30.8 degrees 2Theta (± 0.2 degrees 2Theta).

29. A solid form (form XII) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.5, 9.9, 12.1, 13.6, 16.2, 16.7, 17.1, 17.5, 18.3, 18.5, 20.1, 21.7, 22.4, 23.4, 24.3, 25.6, 26.9 and 31.6 degrees 2Theta (± 0.2 degrees 2Theta).

30. A solid form (form XIII) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.1, 5.8, 6.9, 15.3, 16.2, 17.4, 18.4, 18.9, 19.5, 20.4, 21.1, 21.5, 22.2, 22.6, 25.2 and 25.7 degrees 2Theta (± 0.2 degrees 2Theta).

31. A solid form (form XIV) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.2, 10.2, 12.9, 13.9, 17.1, 17.6, 18.7, 19.8, 20.1, 20.5, 21.0, 21.7, 22.8, 24.1, 25.1, 25.5, 27.1 and 27.4 degrees 2Theta (± 0.2 degrees 2Theta).

32. A solid form (form XV) according to claim 18, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 12.6, 13.8, 14.6, 16.2, 16.6, 17.8, 18.3, 20.4, 20.7, 21.4, 22.4, 23.2, 24.2, 24.5, 25.5, 26.9, 27.8 and 28.7 degrees 2Theta (± 0.2 degrees 2Theta).

33. A solid form designated "pattern 6" according to claim 18, characterized in that it comprises signals in its X-ray powder diffraction curve at positions 7.0, 8.4, 8.9, 13.0, 13.8, 17.7, 18.8, 20.7, 25.8 and 29.7 degrees 2Theta (± 0.2 degrees 2Theta).

34. A solid form (form VIII) according to claim 19, characterized in that it comprises signals in its X-ray powder diffraction curve at positions 5.0, 11.3, 11.6, 12.0, 13.8, 16.2, 16.7, 19.0, 20.1, 20.8, 22.5 and 27.1 degrees 2Theta (± 0.2 degrees 2Theta).

35. A solid form (form XVI) according to claim 19, characterized by its Raman spectrum as presented in Figure 15.

36. The sulfuric acid salt according to claim 20, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 4.7, 6.7, 10.6, 13.3, 14.5, 15.7, 16.4, 18.3, 18.6, 18.9, 19.5, 20.1, 20.9, 21.2, 23.2, 23.7, 24.0, 26.9 and 30.0 degrees 2Theta (± 0.2 degrees 2Theta).

37. The hydrobromic acid salt according to claim 20, characterized by an X-ray powder diffraction pattern comprising characteristic peas at approximately 5.7, 6.8, 11.4, 13.6, 18.1, 19.8, 20.2, 21.4, 21.8, 24.6, 26.1, 27.3 and 29.2 degrees 2Theta (± 0.2 degrees 2Theta).

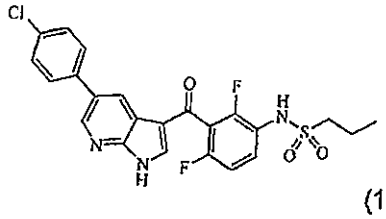
38. The hydrochloric acid salt according to claim 20, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 6.6, 7.8, 11.2, 12.6, 14.1, 14.7, 16.3, 17.8, 19.3, 19.6, 20.7, 21.5, 22.7, 24.1, 25.4 and 25.8 degrees 2Theta (± 0.2 degrees 2Theta).

39. A pharmaceutical composition comprising at least one of the solid forms according to any one of claims 18 to 38, together with pharmaceutically acceptable additives, carriers or excipients.

40. The solid forms, methods of making them, compositions containing them and uses as described herein before.

Claims

1. A solid form of the compound of formula 1,



(1)

wherein said solid form is selected from the group consisting of

a) a substantially amorphous form of compound 1 selected from form XXIV, XXV, XXVI or combinations thereof, wherein the compound 1 is molecularly dispersed;

b) a solvate selected from form III, IV, V, VI, VII, IX, X, XI, XII, XIII, XIV or XV;

c) a polymorph selected from form VIII or XVI; and

d) the sulfuric acid-, hydrobromic acid- or hydrochloric acid salt of compound 1.

2. The solid form of claim 1, selected from a substantially amorphous form of compound 1 selected from form XXIV, XXV, XXVI or combinations thereof, wherein compound 1 is molecularly dispersed within a polymer matrix.

3. The solid form (XXIV) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 27.

4. The solid form (XXV) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 28.

5. The solid form (XXVI) of claim 2, characterized by an X-ray powder diffraction pattern substantially as shown in Fig. 29.

6. The solid form of claim 2, wherein the solid form is prepared by a spray dispersion process.

7. The solid form of claim 2, wherein the polymer is selected from methacrylic acid copolymers, polyvinylpyrrolidone (povidone), 4-vinylpyrrolidone-vinyl acetate copolymer (copovidone) or copolymers of methacrylic acid and ethylacrylate (EUDRAGIT® L100-55).

8. A pharmaceutical composition comprising at least one solid form according to claim 2, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, additives or excipients.

9. The solid form of claim 1, selected from a solvate of form III, IV, V, VI, VII, IX, X, XI, XII, XIII, XIV or XV.

10. The solid form of claim 1, selected from a polymorph of form VIII or XVI.

11. The solid form of claim 1, selected from the sulfuric acid, hydrobromic acid or hydrochloric acid salt of compound 1.

12. A solid form (form III) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 9.5, 10.0, 13.0, 16.7, 18.7, 20.1, 21.0 and 25.6 degrees 2Theta (± 0.2 degrees 2Theta).

13. A solid form (form IV) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.5, 7.4, 11.0, 13.4, 14.8, 16.0, 16.7, 17.1, 17.9, 19.1, 19.5, 20.1, 20.5, 20.9, 21.2, 22.2, 23.0, 23.6, 24.2, 24.5 and 25.1 degrees 2Theta (± 0.2 degrees 2Theta).

14. A solid form (form V) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 12.7, 13.1, 14.3, 16.3, 19.0, 20.1, 22.4, 25.1, 27.1 and 28.9 degrees 2Theta (± 0.2 degrees 2Theta).

15. A solid form (form VI) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.8, 10.3, 11.4, 11.8, 15.1, 15.6, 16.1, 16.6, 18.6, 18.9, 19.2, 20.4, 21.0, 21.6, 22.8, 24.6, 25.1, 25.8, 26.1, 27.4 and 28.8 degrees 2Theta (± 0.2 degrees 2Theta).

16. A solid form (form VII) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.6, 9.4, 9.9, 13.1, 15.9, 16.2, 17.0, 18.1, 18.8, 19.9, 20.5, 20.7, 21.4, 21.8, 24.3, 24.9 and 25.3 degrees 2Theta (± 0.2 degrees 2Theta).

17. A solid form (form IX) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 9.5, 9.9, 13.0, 15.9, 16.4, 17.0, 17.9, 18.7, 19.9, 20.7, 21.7, 24.8 and 25.1 degrees 2Theta (± 0.2 degrees 2Theta).

18. A solid form (form X) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.4, 9.2, 10.8, 13.6, 14.9, 19.0, 20.2, 21.4, 22.4, 23.7, 25.5, 27.0 and 29.8 degrees 2Theta (± 0.2 degrees 2Theta).

19. A solid form (form XI) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 8.0, 12.1, 12.6, 13.4, 13.9, 14.8, 16.2, 17.6, 18.5, 19.2, 20.1, 21.0, 21.4, 21.7, 23.5, 25.3, 25.5, 26.6, 27.0 and 30.8 degrees 2Theta (± 0.2 degrees 2Theta).

20. A solid form (form XII) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 7.5, 9.9, 12.1, 13.6, 16.2, 16.7, 17.1, 17.5, 18.3, 18.5, 20.1, 21.7, 22.4, 23.4, 24.3, 25.6, 26.9 and 31.6 degrees 2Theta (± 0.2 degrees 2Theta).

21. A solid form (form XIII) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.1, 5.8, 6.9, 15.3, 16.2, 17.4, 18.4, 18.9, 19.5, 20.4, 21.1, 21.5, 22.2, 22.6, 25.2 and 25.7 degrees 2Theta (± 0.2 degrees 2Theta).

22. A solid form (form XIV) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.2, 10.2, 12.9, 13.9, 17.1, 17.6, 18.7, 19.8, 20.1, 20.5, 21.0, 21.7, 22.8, 24.1, 25.1, 25.5, 27.1 and 27.4 degrees 2Theta (± 0.2 degrees 2Theta).

23. A solid form (form XV) according to claim 9, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 12.6, 13.8, 14.6, 16.2, 16.6, 17.8, 18.3, 20.4, 20.7, 21.4, 22.4, 23.2, 24.2, 24.5, 25.5, 26.9, 27.8 and 28.7 degrees 2Theta (± 0.2 degrees 2Theta).

24. A solid form designated "pattern 6" according to claim 9, characterized in that it comprises signals in its X-ray powder diffraction curve at positions 7.0, 8.4, 8.9, 13.0, 13.8, 17.7, 18.8, 20.7, 25.8 and 29.7 degrees 2Theta (± 0.2 degrees 2Theta).

25. A solid form (form VIII) according to claim 10, characterized in that it comprises signals in its X-ray powder diffraction curve at positions 5.0, 11.3, 11.6, 12.0, 13.8, 16.2, 16.7, 19.0, 20.1, 20.8, 22.5 and 27.1 degrees 2Theta (± 0.2 degrees 2Theta).

26. A solid form (form XVI) according to claim 10, characterized by its Raman spectrum as presented in Figure 15.

27. The sulfuric acid salt according to claim 11, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 4.7, 6.7, 10.6, 13.3, 14.5, 15.7, 16.4, 18.3, 18.6, 18.9, 19.5, 20.1, 20.9, 21.2, 23.2, 23.7, 24.0, 26.9 and 30.0 degrees 2Theta (± 0.2 degrees 2Theta).

28. The hydrobromic acid salt according to claim 11, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 5.7, 6.8, 11.4, 13.6, 18.1, 19.8, 20.2, 21.4, 21.8, 24.6, 26.1, 27.3 and 29.2 degrees 2Theta (± 0.2 degrees 2Theta).

29. The hydrochloric acid salt according to claim 11, characterized by an X-ray powder diffraction pattern comprising characteristic peaks at approximately 6.6, 7.8, 11.2, 12.6, 14.1, 14.7, 16.3, 17.8, 19.3, 19.6, 20.7, 21.5, 22.7, 24.1, 25.4 and 25.8 degrees 2Theta (± 0.2 degrees 2Theta).

30. A pharmaceutical composition comprising at least one of the solid forms according to claim 9, together with pharmaceutically acceptable additives, carriers or excipients.