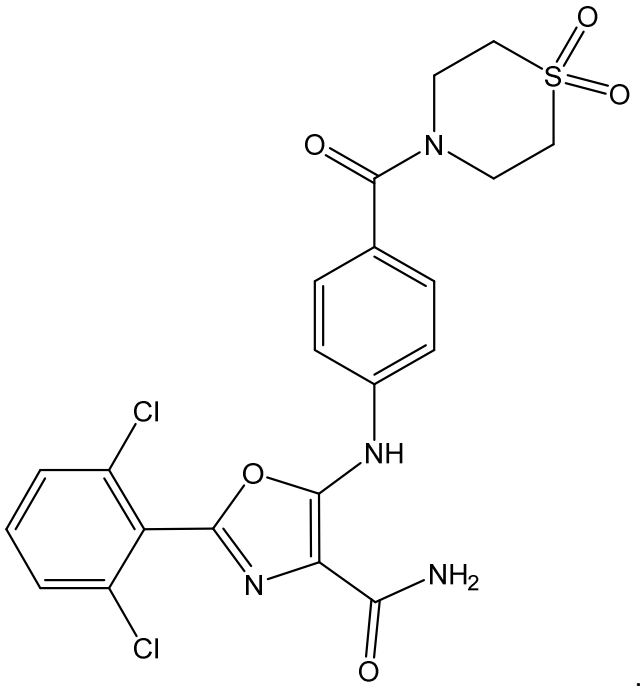
CLAIMS

1. A crystalline form of a compound having the formula **(1)**:

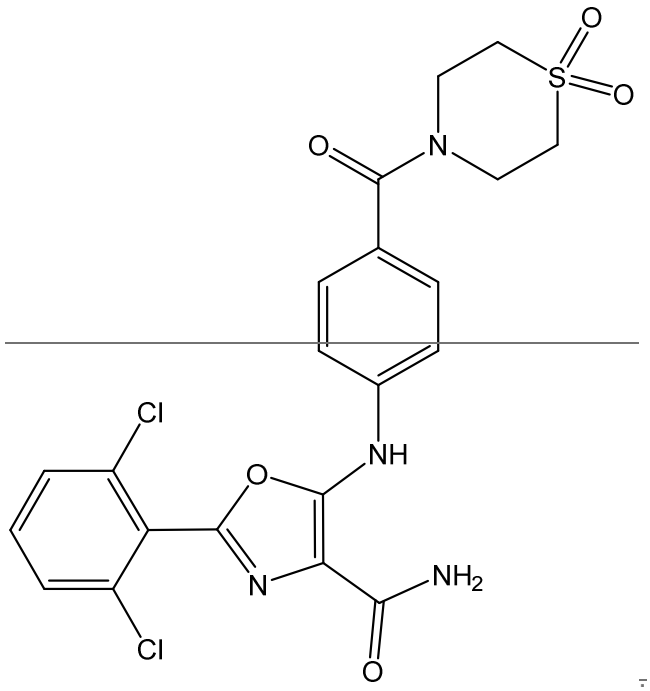


.

wherein the crystalline form has a crystalline purity of at least 90%~~, more preferably at least 95%~~.

2. A crystalline form of a compound having the formula **(1)**, wherein the crystalline form has a crystalline purity of at least 95%.

~~2. A crystalline form of a compound having the formula **(1)**:~~



~~which is of Form A as defined herein.~~

~~3. A substantially crystalline form (Form A) of the compound of formula **(1)** according to claim 2 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.1º and/or 12.3º and/or 16.7º and/or 20.7º and/or 13.7°.~~

~~4. A substantially crystalline form (Form A) of the compound of formula **(1)** according to claim 3 having an X-ray powder diffraction pattern characterised by the presence of major peaks at two or more, e.g. three or more, or four or more, and in particular five diffraction angles (2θ) selected from 23.1º, 12.3º, 16.7º, 20.7º and 13.7° (±0.2º).~~

~~5. A substantially crystalline form (Form A) of the compound of formula **(1)** according to any one of claims 2 to 4 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.1º and/or 12.3º and/or 16.7º and/or 20.7º and/or 13.7° (e.g. at least four and more particularly at least five of the diffraction angles), and optionally one or more further peaks at diffraction angles (2θ) selected from 21.9°, 20.8°, 10.7°, 23.6° and 21.4° (±0.2º).~~

~~6. A method for the preparation of a substantially crystalline form (Form A) of compound (1) as defined in any one of claims 2 to 5 which method comprises:~~

(i) dispersing an amorphous form of compound (1) in an aqueous solvent selected from water, water/acetonitrile (e.g. 4:1 MeCN/water) and water/THF (e.g. 4:1 THF/water) to form a mixture;

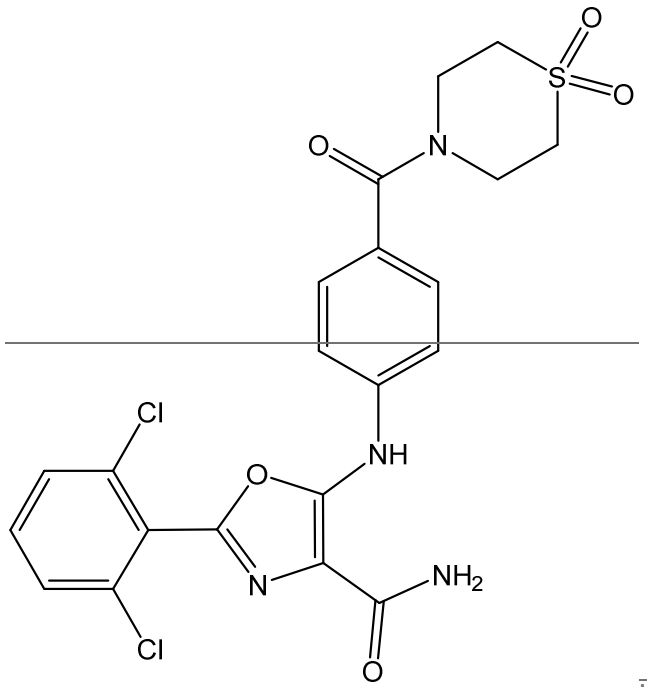
(ii) heating the mixture to a moderately elevated temperature in the range from 45-65 °C and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 17 hours);

(iii) cooling or allowing the cooling of the mixture from the moderately elevated temperature to a lower temperature in the range from 15-30 °C (e.g. 20-30 °C such as approximately 25 °C) and holding the mixture at the lower temperature for a period of at least 2 hours (e.g. 2 to 8 hours such as approximately 4.5 hours); and

(iv) optionally subjecting the mixture to a further heating and cooling cycle comprising heating the mixture to a moderately elevated temperature in the range from 45-65 °C and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 16 hours); cooling the mixture to a lower temperature in the range from 15-30 °C (e.g. 20-30 °C such as approximately 25 °C) and optionally holding the mixture at the lower temperature for a period of at least half an hour (e.g. up to approximately 1 hour); and

(v) isolating (e.g. by filtration) the crystalline Form A of compound (1) thus formed.

7. A crystalline form of a compound having the formula **(1)**:



~~which is of Form B as defined herein.~~

~~3~~8. A substantially crystalline form ~~(Form B)~~ of the compound of formula **(1)** according to claim 1 or claim 2 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.2º and/or 16.7º and/or 22.6º and/or 26.6º and/or 12.0°.

~~4~~9. A substantially crystalline form ~~(Form B)~~ of the compound of formula **(1)** according to claim ~~3~~7 having an X-ray powder diffraction pattern characterised by the presence of major peaks at two or more, e.g. three or more, or four or more, and in particular five diffraction angles (2θ) selected from 23.2º, 16.7º, 22.6º, 26.6º and 12.0° (±0.2º).

~~5~~10. A substantially crystalline form ~~(Form B)~~ of the compound of formula **(1)** according to claim ~~4~~9 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.2º and/or 16.7º and/or 22.6º and/or 26.6º and/or 12.0° (e.g. at least four and more particularly at least five of the diffraction angles), and optionally one or more further peaks at diffraction angles (2θ) selected from 23.4°, 25.3°, 7.1°, 19.9° and 27.8° (±0.2º).

6. A substantially crystalline form of the compound of formula **(1)** according to claim 3 having an X-ray powder diffraction pattern characterized by the presence of major peaks at the diffraction angles (2θ) 23.2º, 16.7º, 22.6º, 26.6º and 12.0°, and one or more further peaks at diffraction angles (2θ) selected from 23.4°, 25.3°, 7.1°, 19.9° and 27.8°

(±0.2º), and one or more further peaks at diffraction angles (2θ) selected from 14.2°, 27.0°, 24.1°, 28.9° and 14.5° (±0.2º).

711. A method for the preparation of a substantially crystalline form (Form B) of compound (1) as defined in any one of claims 37 to 610, which method comprises:

(i) dispersing an amorphous form of compound (1) in a solvent selected from hydrocarbon solvents, halogenated hydrocarbon solvents (other than dichloromethane), methanol, isopropyl alcohol, aliphatic ketones (e.g. C_{1-8} ketones), non-aromatic ethers (e.g. C_{3-6} dialkyl and alkylcycloalkyl ethers and THF), and isopropylacetate to form a mixture;

(ii) heating the mixture to a moderately elevated temperature in the range from 45-65 °C and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 17 hours);

(iii) cooling or allowing the cooling of the mixture from the moderately elevated temperature to a lower temperature in the range from 15-30 °C (e.g. 20-30 °C such as approximately 25 °C) and holding the mixture at the lower temperature for a period of at least 2 hours (e.g. 2 to 8 hours such as approximately 4.5 hours); and

(iv) optionally subjecting the mixture to a further heating and cooling cycle comprising heating the mixture to a moderately elevated temperature in the range from 45-65 °C and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 16 hours); cooling the mixture to a lower temperature in the range from 15-30 °C (e.g. 20-30 °C such as approximately 25 °C) and optionally holding the mixture at the lower temperature for a period of at least half an hour (e.g. up to approximately 1 hour); and

(v) isolating (e.g. by filtration) the crystalline Form B of compound (1) thus formed.

812. A method for the preparation of a substantially crystalline form (Form B) of compound (1) as defined in any one of claims 37 to 610, which method comprises:

(i) dispersing a solid form of compound (1) in methylethylketone (MEK) to form a mixture;

(ii) subjecting the mixture to an equilibration procedure comprising periods of heating and cooling the mixture until a suspension of crystalline compound (1) Form B is formed; and optionally further equilibrating the mixture until a desired level of polymorphic purity is achieved.

9. A substantially crystalline form of the compound of formula **(1)** according to claim 1 or claim 2 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.1º and/or 12.3º and/or 16.7º and/or 20.7º and/or 13.7°.

10. A substantially crystalline form of the compound of formula **(1)** according to claim 9 having an X-ray powder diffraction pattern characterised by the presence of major peaks at two or more, e.g. three or more, or four or more, and in particular five diffraction angles (2θ) selected from 23.1º, 12.3º, 16.7º, 20.7º and 13.7° (±0.2º).

11. A substantially crystalline form of the compound of formula **(1)** according to any one of claims 9 or 10 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 23.1º and/or 12.3º and/or 16.7º and/or 20.7º and/or 13.7° (e.g. at least four and more particularly at least five of the diffraction angles), and optionally one or more further peaks at diffraction angles (2θ) selected from 21.9°, 20.8°, 10.7°, 23.6° and 21.4° (±0.2º).

12. A method for the preparation of a substantially crystalline form of compound (1) as defined in any one of claims 9 to 11 which method comprises:

(i) dispersing an amorphous form of compound (1) in an aqueous solvent selected from water, water/acetonitrile (e.g. 4:1 MeCN/water) and water/THF (e.g. 4:1 THF/water) to form a mixture;

(ii) heating the mixture to a moderately elevated temperature in the range from 45-65 ℃ and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 17 hours);

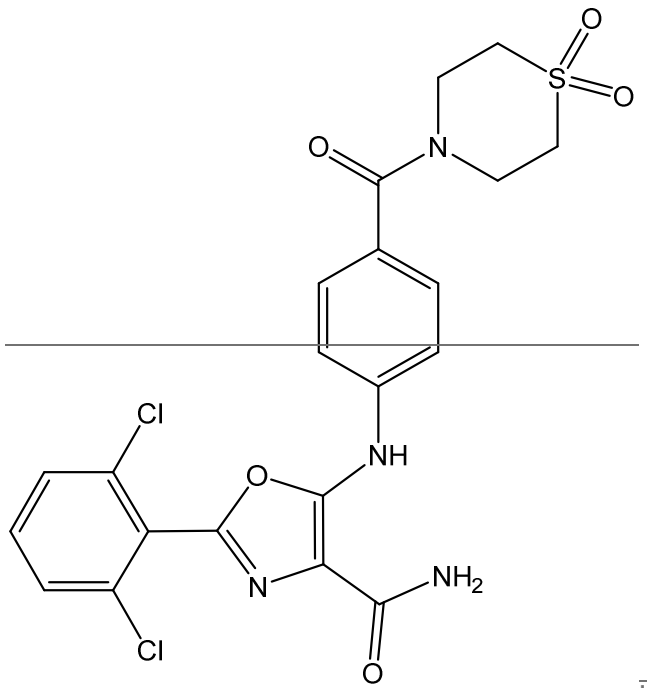
(iii) cooling or allowing the cooling of the mixture from the moderately elevated temperature to a lower temperature in the range from 15-30 ℃ (e.g. 20-30 ℃ such as approximately 25 ℃) and holding the mixture at the lower temperature for a period of at least 2 hours (e.g. 2 to 8 hours such as approximately 4.5 hours); and

(iv) optionally subjecting the mixture to a further heating and cooling cycle comprising heating the mixture to a moderately elevated temperature in the range from 45-65 ℃ and holding the mixture at the moderately elevated temperature for a period of at least 10 hours (for example from 10 to 25 hours, e.g. about 16 hours); cooling the mixture to a lower temperature in the range from 15-30 ℃ (e.g. 20-30 ℃ such as approximately 25

°C) and optionally holding the mixture at the lower temperature for a period of at least half an hour (e.g. up to approximately 1 hour); and

(v) isolating (e.g. by filtration) the crystalline compound (1) thus formed.

~~13. A crystalline form of a compound having the formula **(1)**:~~

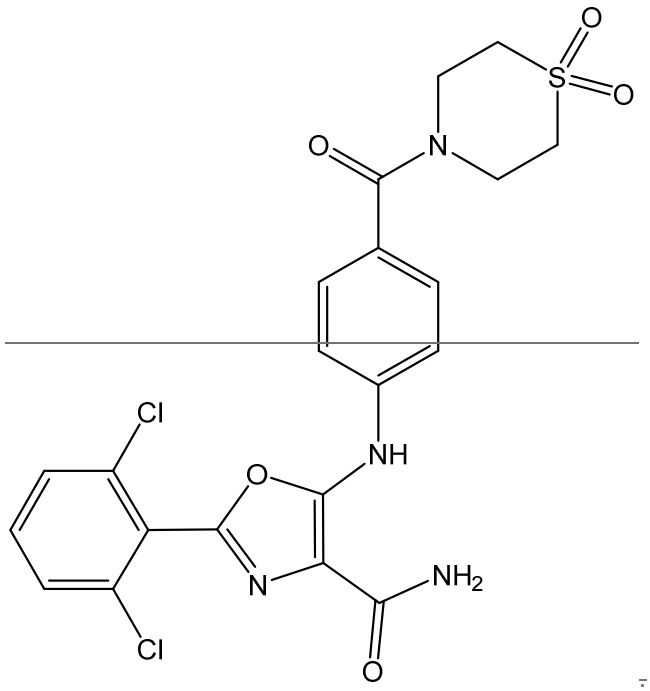


~~which is of Form C as defined herein.~~

1~~3~~4. A substantially crystalline form ~~(Form C)~~ of the compound of formula **(1)** according to claim 1~~13~~ or claim 2 having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 12.8° and/or 17.8° and/or 22.9° and/or 24.3° and/or 8.5º.

1~~4~~5. A substantially crystalline form ~~(Form C)~~ of the compound of formula **(1)** according to claim 13~~14~~ having an X-ray powder diffraction pattern characterised by the presence of major peaks at the diffraction angles (2θ) 12.8° and/or 17.8° and/or 22.9° and/or 24.3° and/or 8.5º (e.g. at least four and more particularly at least five of the diffraction angles), and optionally one or more further peaks at diffraction angles (2θ) selected from 13.0°, 20.1°, 16.5°, 26.1° and 22.4° (±0.2º).

~~16. A crystalline form of a compound having the formula **(1)**:~~



~~which is of Form D as defined herein.~~

15~~7~~. A pharmaceutical composition comprising a crystalline form of a compound having the formula **(1)** as defined in any one of claims 1 to ~~6~~5, ~~9~~7 to 11~~10~~ and 13 to 14~~16~~ and a pharmaceutically acceptable excipient.

~~18. An invention as defined in any one of Embodiments 1.0 to 1.20, 2.1 to 2.21, 3.1 to 3.15, 4.1 to 4.15, 5.1, 5.2, 6.1 to 6.15, 7.1 to 7.12, and 8.1 to 8.3.~~

16. A compound having the formula **(1)** as defined in any one of claims 1 to 6, 9 to 11 and 13 to 14 for use in medicine.

17. The use of a compound having the formula **(1)** as defined in any one of claims 1 to 6, 9 to 11 and 13 to 14 for the manufacture of a medicament for the treatment of:

a) diseases mediated by TYK2;

b) an inflammatory or immune disorder; or

c) an autoimmune disease.