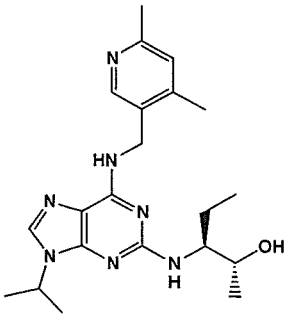
STATEMENT OF INVENTION

Disclosed is a crystalline form of compound (I),

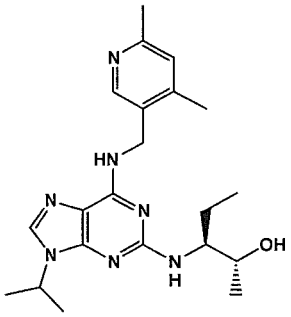


(I)

wherein said compound is in the form of the free base or a pharmaceutically acceptable salt thereof, or a solvated form of the free base or salt form thereof.

The crystalline forms of the disclosure typically demonstrate one or more improved properties over the amorphous form. Suitable properties include, for example, better storage stability, improved ease of handling (flowability, compressibility, stability), easier purification, and easier synthetic scale up

In one aspect, the present invention provides a crystalline form of compound (I),



(I)

wherein said compound is in the form of the free base or a solvate thereof, which is characterized by an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 9.60 ± 0.2, 10.22 ± 0.2, 11.29 ± 0.2, 11.66 ± 0.2, 12.26 ± 0.2, 12.62 ± 0.2, 13.17 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2, 15.15 ± 0.2, 15.57 ± 0.2, 16.99 ± 0.2, 17.68 ± 0.2, 18.30 ± 0.2, 18.39 ± 0.2, 18.63 ± 0.2, 18.97 ± 0.2, 19.32 ± 0.2 and 20.20 ± 0.2.

Also disclosed is a pharmaceutical composition comprising a crystalline form as described above as an active ingredient and a pharmaceutically acceptable diluent, excipient or carrier.

In another aspect, the present invention provides a pharmaceutical composition comprising the crystalline form disclosed herein and a pharmaceutically acceptable carrier, diluent or excipient

In yet another aspect, the present invention provides a crystalline form as disclosed herein for use in medicine.

Also disclosed is a crystalline form as described above for use in the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

In yet another aspect, the present invention provides the use of a crystalline form disclosed herein in the preparation of a medicament for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders,

neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

Also disclosed is a method for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders, said method comprising administering a pharmacologically effective amount of a crystalline form as described above to a subject in need thereof.

Also disclosed are processes for preparing crystalline forms as described above.

In yet another aspect, the present invention provides a process for preparing crystalline free base of compound (I) disclosed herein, said method comprising the steps of crystallising compound (I) in free base form from methyl t-butyl ether (MTBE).

DETAILED DESCRIPTION

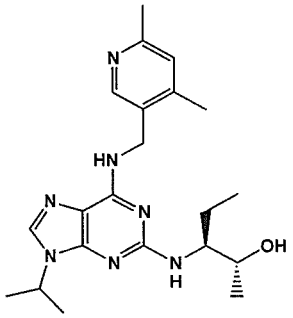
The crystalline forms of the invention may be characterised by a range of different analytical techniques, including x-ray powder diffraction and differential scanning calorimetry. Further details of these techniques and equipment are set forth in the accompanying examples section.

As used herein, the term "solvate" or "solvated form" refers to a crystal having one or more molecules of solvent associated therewith as an inherent part of the crystal structure. Preferably, the solvate or solvated form is the hydrate.

In general, different plural crystalline forms (polymorphs) of the same compound can be produced by varying the crystallisation conditions used. These different crystalline forms have different three-dimensional structures and different physicochemical properties. However, the existence of polymorphs is inherently unpredictable and theoretical calculations to predict polymorphs are extremely unreliable, with many more polymorphs predicted than can actually be isolated in practice.

CLAIMS

1. A crystalline form of compound (I),



(I)

wherein said compound is in the form of the free base or a solvate thereof, which is characterized by an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 9.60 ± 0.2, 10.22 ± 0.2, 11.29 ± 0.2, 11.66 ± 0.2, 12.26 ± 0.2, 12.62 ± 0.2, 13.17 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2, 15.15 ± 0.2, 15.57 ± 0.2, 16.99 ± 0.2, 17.68 ± 0.2, 18.30 ± 0.2, 18.39 ± 0.2, 18.63 ± 0.2, 18.97 ± 0.2, 19.32 ± 0.2 and 20.20 ± 0.2.

2. A crystalline form according to claim 1 wherein the x-ray powder diffraction pattern comprises two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 12.26 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2 and 15.57 ± 0.2.

3. A crystalline form according to any preceding claim, which is characterized by an x-ray powder diffraction pattern in which the peak positions are substantially in accordance with the 2[theta] peak positions recited in the table below:

Pos. [°2Th.]	Height [cts]	FWHM [°2Th.]	d-spacing [Å]	Rel. Int. [%]	Tip width [°2Th.]
7.5313	21162.64	0.0768	11.73852	100.00	0.0921
9.6026	846.92	0.0768	9.21066	4.00	0.0921
10.2275	400.15	0.1023	8.64925	1.89	0.1228
11.2954	1863.94	0.1023	7.83384	8.81	0.1228
11.6652	300.53	0.1023	7.58631	1.42	0.1228
12.2672	3812.02	0.1023	7.21534	18.01	0.1228
12.6242	497.83	0.1023	7.01205	2.35	0.1228
13.1780	953.85	0.1023	6.71859	4.51	0.1228
14.0653	4092.77	0.1023	6.29672	19.34	0.1228
14.8535	1458.15	0.0768	5.96431	6.89	0.0921
15.1515	343.64	0.0768	5.84765	1.62	0.0921
15.5775	2894.50	0.1279	5.68868	13.68	0.1535
16.9914	2108.17	0.1023	5.21838	9.96	0.1228
17.6862	1501.97	0.1279	5.01490	7.10	0.1535
18.3040	644.51	0.0591	4.84701	3.05	0.0709
18.3954	1212.49	0.0768	4.82314	5.73	0.0921
18.6301	1666.18	0.1023	4.76289	7.87	0.1228
18.9784	1639.81	0.1279	4.67626	7.75	0.1535
19.3292	475.31	0.1023	4.59219	2.25	0.1228
20.2061	1067.39	0.1023	4.39483	5.04	0.1228

4. A crystalline form according to any preceding claim, which is characterized by a differential scanning calorimetry trace recorded at a heating rate of 20°C per minute which shows a maximum endothermic peak at a temperature between about 130°C and about 140°C.

5. A crystalline form according to any preceding claim, which is monoclinic P21/c space group with unit cell dimensions of a = 15.19 ± 2 Å, b = 18.34 ± 2 Å, c = 8.65 ± 2 Å and [beta] = 95.53 ± 2°.

6. A pharmaceutical composition comprising the crystalline form according to any one of claims 1 to 5 and a pharmaceutically acceptable carrier, diluent or excipient.

7. A crystalline form according to any one of claims 1 to 5 for use in medicine.

8. A crystalline form according to any one of claims 1 to 5 for use in the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

9. Use of a crystalline form according to any one of claims 1 to 5 in the preparation of a medicament for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

10. A process for preparing crystalline free base of compound (I) according to claim 1, said method comprising the steps of crystallising compound (I) in free base form from methyl t-butyl ether (MTBE).

CRYSTALLINE FORMS OF A PURINE DERIVATIVE

Abstract

The present invention relates to new crystalline forms of a purine derivative which exhibits excellent anti-tumour activity. The invention also relates to a pharmaceutical composition containing said crystalline forms as an active ingredient, and use thereof in the prevention or treatment of disease. The invention further relates to a process for preparing the crystalline forms.

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