Patent Claims

1) Solid preparation comprising micronized 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or a pharmaceutical acceptable salt thereof and a filler, wherein 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or its pharmaceutically acceptable salt is present from 20 to 80 % (w/w) based upon the total weight of the solid preparation, wherein the solid preparation is prepared by dry granulation.

2) The solid preparation according to Claim 1, wherein 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile is present in the form of its sulphate, phosphate, mesylate, besylate, tosylate, fumarate, monohydrochloride or maleate salt.

3) The solid preparation according to Claim 1 or 2, wherein the pharmaceutically acceptable salt of 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile is a hydrate of the respective salt.

4) The solid preparation according to any one of Claims 1 to 3, wherein the 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile is present in the form of its monohydrochloride monohydrate salt.

5) The solid preparation according to any one of Claims 1 to 4, wherein 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile has a mean particle size that is characterized by a d50 value in the range from 5 µm to 80 µm.

6) The solid preparation according to any one of Claims 1 to 5, wherein the 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile has a mean particle size that is characterized by a d50 value in the range from 5 µm to 50 µm.

7) The solid preparation according to any one of Claims 1 to 6, wherein the 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile has a mean particle size that is characterized by a d50 value in the range from 5 µm to 25 µm.

8) The solid preparation according to any one of Claims 1 to 7, wherein the filler is a sugar, a sugar alcohol, or dicalcium phosphate.

9) The solid preparation according to Claim 8, wherein the filler is a sugar alcohol.

10) The solid preparation according to Claim 9, wherein the sugar alcohol is sorbitol, mannitol, dulcitol, xylitol or ribitol.

11) The solid preparation according to Claim 10, wherein the sugar alcohol is mannitol.

12) The solid preparation according to any one of Claims 1 to 11, wherein the solid preparation further comprises a binder.

13) The solid preparation according to Claim 12, wherein the binder is polyvinylpyrrolidone, polyvinyl acetate, a vinylpyrrolidone-vinyl acetate copolymer, polyethylene glycol, a starch paste such as maize starch paste, or a cellulose derivative such as hydroxypropyl methylcellulose, hydroxypropyl cellulose or microcrystalline cellulose, preferably microcrystalline cellulose.

14) The solid preparation according to any one of Claims 1 to 13, wherein the solid preparation further comprises a lubricant.

15) The solid preparation according to Claim 14, wherein the lubricant is sodium stearyl fumarate, esters of glycerol with fatty acids, stearic acid, or pharmaceutically acceptable salts of stearic acid and divalent cations, preferably magnesium stearate.

16) The solid preparation according to any one of Claims 1 to 15, wherein the solid preparation has a mean particle size that is characterized by a d50 value in the range from 50 µm to 1 mm, preferably from 60 µm to 800 µm and more preferably from 70 to 600 µm.

17) A pharmaceutical preparation comprising the solid preparation according to any one of Claims 1 to 16.

18) The pharmaceutical preparation according to Claim 17, which is a pharmaceutical preparation for oral administration.

19) The pharmaceutical preparation according to Claim 17 or 18, which is an immediate release preparation.

20) The pharmaceutical preparation according to any one of Claims 17 to 19, which is a capsule comprising the solid preparation according to any one of Claims 1 to 16 and optionally further comprising one or more pharmaceutically acceptable excipients.

21) The pharmaceutical preparation according to Claim 20, which is a capsule, which contains 40 to 100 % (w/w) of the solid preparation according to any one of claims 1 to 16; and 0 to 60 % (w/w) of at least one pharmaceutically acceptable excipient, preferably selected from a filler, a glidant, a disintegrant and a lubricant, based upon the total weight of all material contained in the capsule.

22) The pharmaceutical preparation according to any one of Claims 17 to 19, which is a tablet and which in addition to the pharmaceutically acceptable excipients present in the solid preparation optionally comprises one or more pharmaceutically acceptable excipient selected from a filler, a disintegrant, a glidant and a lubricant.

23) The pharmaceutical preparation according to Claim 22, which is a tablet comprising the solid preparation according to any one of claims 1 to 16 and

optionally further excipients, which tablet, based upon its total weight, comprises:

i) 20 to 80 % (w/w) of 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or a pharmaceutically acceptable salt thereof;

ii) 10 to 70 % (w/w) of a filler;

iii) 0 to 20 % (w/w) of a binder;

iv) 0 to 20 % (w/w) of disintegrant;

v) 0 to 5 % (w/w) of a lubricant;

vi) 0 to 7.5 % (w/w) of glidant; and

vii) a total of 0 to 20 % (w/w) of one or more additional pharmaceutically acceptable excipients.

24) The pharmaceutical preparation according to Claim 22 or 23, which is a tablet comprising the solid preparation according to any one of claims 1 to 16 and optionally further excipients, which tablet, based upon its total weight, comprises:

i) 30 to 70 % (w/w) of 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or a pharmaceutically acceptable salt thereof;

ii) 20 to 60 % (w/w) of a filler;

iii) 0 to 10 % (w/w) of a binder;

iv) 0.25 to 10 % (w/w) of disintegrant;

v) 0 to 4 % (w/w) of a lubricant;

vi) 0 to 5 % (w/w) of a glidant; and

vii) a total of 0 to 10 % (w/w) of one or more additional pharmaceutically acceptable excipients.

25) The pharmaceutical preparation according to Claim 22, 23 or 24, which is a tablet comprising:

i) 35 to 60 % (w/w) of 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or a pharmaceutically acceptable salt thereof;

ii) 40 to 60 % (w/w) of a filler;

iii) 0 to 5 % (w/w) of a binder;

iv) 0.5 to 5 % (w/w) of disintegrant;

v) 0.25 to 3 % (w/w) of a lubricant;

vi) 0 to 2 % (w/w) of a glidant; and

vii) a total of 0 to 10 % (w/w) of one or more additional pharmaceutically acceptable excipients.

26) The pharmaceutical preparation according to any one of claims 22 to 25, wherein the filler is mannitol, the binder is microcrystalline cellulose, the disintegrant is selected from crospovidone, carboxy starch glycolate, carboxymethylcellulose and salts and derivatives thereof, especially croscarmellose sodium, the lubricant is selected from magnesium stearate, calcium stearate, stearic acid, glycerol fatty acid esters and sodium stearyl fumarate and/or the glidant is selected from colloidal silicon dioxide and derivatives thereof.

27) The pharmaceutical preparation according to Claim 26, wherein the filler is mannitol, the binder is microcrystalline cellulose, the disintegrant is crospovidone, the lubricant is magnesium stearate, and the glidant is colloidal silicon dioxide.

28) A method for preparing the solid preparation according to any one of Claims 1 to 16, the method comprising the steps of:

(a) mixing 3-(1-{3-[5-(1-Methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile or a pharmaceutically acceptable salt thereof and a filler and optionally one or more further pharmaceutically acceptable excipients;

(b) dry granulating the mixture prepared by step (a) to form the solid preparation; and

(c) optionally milling.

29) The method for preparing the solid preparation according to Claim 28, wherein dry granulating is roller compacting.

30) A method for preparing a pharmaceutical preparation, which is a tablet, comprising the steps of:

(a) conducting the method according to Claim 28 or 29 to form the solid preparation according to any one of claims 1 to 16;

(b) mixing the solid preparation and one or more pharmaceutically acceptable excipients;

(c) tableting the mixture prepared by step (b); and

(d) optionally film coating of the tablets prepared by step (c).

31) A method for preparing a pharmaceutical preparation, which is a capsule, comprising the steps of:

(a) conducting the method according to Claim 28 or 29 to form the solid preparation according to any one of claims 1 to 16;

(b) optionally mixing the solid preparation and one or more pharmaceutically acceptable excipient; and

(c) filling the solid preparation prepared by step (a) or the mixture prepared by step (b) into capsules.

32) Use of the pharmaceutical preparation according to any one of Claims 17 to 27 in the manufacture of a medicament for the treatment of cancer.

33) The use according to Claim 32, wherein the treatment further comprises radiotherapy.

34) The use according to Claim 32 or 33, wherein the treatment further comprises chemotherapy.

35) The use according to any one of Claims 32 to 34, wherein the treatment further comprises immunotherapy.

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