

CLAIMS

1. A crystalline form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide Form A characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of $(5.0 \pm 0.2)^\circ$, $(15.2 \pm 0.2)^\circ$, $(19.7 \pm 0.2)^\circ$, and $(22.1 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.
2. The crystalline form according to claim 1 characterized by having a powder X-ray diffractogram comprising additional reflections at 2-Theta angles of $(8.8 \pm 0.2)^\circ$, $(17.4 \pm 0.2)^\circ$, $(17.6 \pm 0.2)^\circ$ and $(24.5 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm; or:
characterized by having a powder X-ray diffractogram comprising additional reflections at 2-Theta angles of $(8.8 \pm 0.2)^\circ$, ~~$(15.2 \pm 0.2)^\circ$~~ , $(17.1 \pm 0.2)^\circ$, $(17.4 \pm 0.2)^\circ$, $(17.6 \pm 0.2)^\circ$, $(22.8 \pm 0.2)^\circ$ and $(24.5 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.
3. The crystalline form according to claim 1 or claim 2 characterized by having a powder X-ray diffractogram comprising additional reflections at 2-Theta angles of $(9.8 \pm 0.2)^\circ$, $(10.1 \pm 0.2)^\circ$, $(11.4 \pm 0.2)^\circ$, $(13.2 \pm 0.2)^\circ$, $(18.5 \pm 0.2)^\circ$, ~~$(19.7 \pm 0.2)^\circ$~~ , $(20.3 \pm 0.2)^\circ$, $(25.9 \pm 0.2)^\circ$ and $(26.7 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm; and/or:
characterized by having a differential scanning calorimetry curve comprising an endothermic peak having an peak temperature of $(175.2 \pm 0.5)^\circ\text{C}$, when measured at a heating rate of 10 K/min; and/or:
characterized by having a thermogravimetric analysis curve showing a mass loss of not more than 0.01 weight%, based on the weight of the crystalline form, when heated from 30 °C to 180 °C at a rate of 10 K/min.

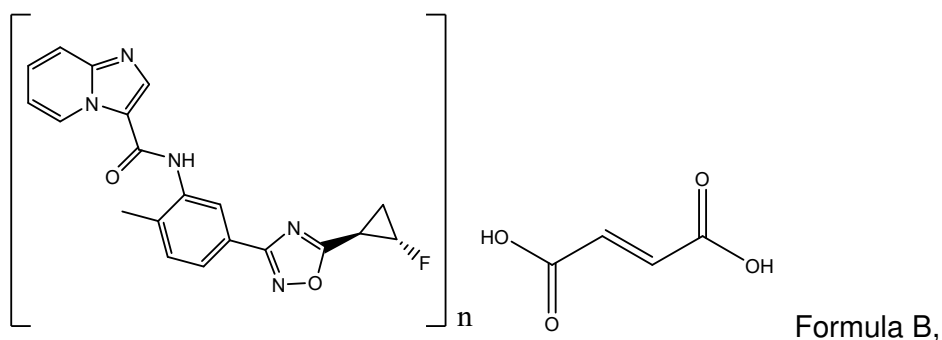
4. The crystalline form as defined in any one of the preceding claims characterized by showing a mass change of not more than 0.2 w-% based on the weight of the crystalline form, when measured with gravimetric moisture sorption at a relative humidity in the range of from 10 to 100% and a temperature of $(25 \pm 1) ^\circ\text{C}$.
5. A salt or co-crystal of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide with fumaric acid.
6. The co-crystal of claim 5 wherein the molar ratio of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide to fumaric acid is 1.8-2.2 :1; or:

wherein the molar ratio of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide to fumaric acid is 1.9-2.1 :1; or:

wherein the molar ratio of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide to fumaric acid is 1.95-2.05 :1; or:

wherein the molar ratio of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide to fumaric acid is 2:1; or:

said co-crystal characterized by having the chemical structure according to formula B



wherein n is in the range selected from 1.8 to 2.2; 1.9 to 2.1; 1.95 to 2.05 or 2.0.

7. The co-crystal according to claim 5 or claim 6 characterized by having a powder X-ray diffractogram (PXRD) comprising reflections at 2-Theta angles of $(12.3 \pm 0.2)^\circ$, $(14.9 \pm 0.2)^\circ$, $(15.6 \pm 0.2)^\circ$, and $(27.3 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

8. The co-crystal of claim 7 characterized by having a powder X-ray diffractogram (PXRD) comprising additional reflections at 2-Theta angles of ~~$(14.9 \pm 0.2)^\circ$~~ , $(16.5 \pm 0.2)^\circ$, $(21.2 \pm 0.2)^\circ$ and $(25.4 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm; and/or:

characterized by having a powder X-ray diffractogram (PXRD) comprising additional reflections at 2-Theta angles of $(4.9 \pm 0.2)^\circ$, $(10.0 \pm 0.2)^\circ$, $(11.5 \pm 0.2)^\circ$, $(15.6 \pm 0.2)^\circ$, $(18.6 \pm 0.2)^\circ$, $(20.1 \pm 0.2)^\circ$, $(22.6 \pm 0.2)^\circ$, $(22.8 \pm 0.2)^\circ$ and $(26.5 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

9. The co-crystal according to any one of claims 5 to 8 characterized by having a differential scanning calorimetry (DSC) curve comprising an endothermic peak having an onset temperature of $(227 \pm 1)^\circ\text{C}$, when measured at a heating rate of 10 K/min; or:

characterized by having a differential scanning calorimetry (DSC) curve comprising an endothermic peak having an peak temperature of $(229 \pm 1)^\circ\text{C}$, when measured at a heating rate of 10 K/min.

10. The co-crystal according to any one of claims 5 to 9 characterized by having a thermogravimetric analysis (TGA) curve showing a mass loss of not more than 2.5 weight%, based on the weight of the co-crystal, when heated from 30 °C to 200 °C at a rate of 10 °C/min; and/or:

characterized by showing a mass change of not more than 0.2 w-% based on the weight of the co-crystal, when measured with gravimetric moisture sorption at a relative humidity in the range of from 10 to 100% and a temperature of $(25 \pm 1)^\circ\text{C}$.

11. A composition comprising the crystalline form as defined in any one of the preceding claims and at most 20 weight%, 10 weight%, 5 weight%, 2 weight% or 1 weight% of any other solid-state form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide, based on the weight of the composition; optionally:

wherein the crystalline form is a co-crystal of any one of claims 8- 9 and the other solid-state form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide is Form A characterized by having a powder X-ray diffractogram (PXRD) comprising reflections at 2-Theta angles of $(13.2 \pm 0.2)^\circ$ and $(19.7 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm; or:

wherein the other solid-state form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide is Form HA characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of $(12.8 \pm 0.2)^\circ$ and $(13.6 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm; or:

wherein the other physical form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide is Form HB characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of $(6.7 \pm 0.2)^\circ$ and $(18.0 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

12. Use of the crystalline form as defined in any one of claims 1 to 10 or the composition as defined in claim 11 for the preparation of a pharmaceutical composition.

13. A pharmaceutical composition comprising the crystalline form as defined in any one of claims 1 to 10 or the composition as defined in claim 11 and at least one pharmaceutically acceptable excipient; optionally wherein the pharmaceutical composition is an oral solid dosage form.
14. The crystalline form as defined in any one of claims 1 to 10 or the composition as defined in claim 11 or the pharmaceutical composition according to claim 13 for use as a medicament; or:

for use in the treatment and/or prophylaxis of asthma, allergic rhinitis, pulmonary arterial hypertension (PAH), pulmonary fibrosis, hepatic fibrosis, cardiac fibrosis, scleroderma, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), urticaria, dermatosis, atopic dermatitis, allergic contact dermatitis, rheumatoid arthritis, multiple sclerosis, melanoma, a gastrointestinal stromal tumor, a mast cell tumor, mastocytosis, anaphylactic syndrome, type I diabetes or type II diabetes; or:

for use in the treatment and/or prophylaxis of urticaria.
15. A process for the preparation of the crystalline form as defined in any one of claims 1 to 4 or the composition as defined in claim 11 comprising:
 - (i) providing N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide in solid form;
 - (ii) dissolving N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide provided in step (i) in a solvent under mechanical stirring at elevated temperature;
 - (iii) cooling the solution from (ii) to room temperature under mechanical stirring;
 - (iv) separating at least a part of the crystals obtained in step (iii) from the mother liquor;
 - (v) optionally washing the isolated crystals obtained in step (iv); and
 - (vi) drying the crystals obtained in step (iii) or (iv).

16. A process for the preparation of the co-crystal as defined in any one of claims 5 to 10 or the composition as defined in claim 11 comprising:

- (a) slurring a powder mixture of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide and fumaric acid in a solvent;
- (b) heating the suspension provided in (a) under stirring;
- (c) cooling the suspension in (b) to room temperature under stirring;
- (d) separating at least a part of the crystals obtained in (b) or (c) from the mother liquor;
- (e) washing the isolated crystals obtained in (d); and
- (f) optionally, drying the crystals obtained in any one of steps (d) or (e).

17. A crystalline form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide Form HA characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of $(12.8 \pm 0.2)^\circ$ and $(13.6 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.

18. A crystalline form of N-(5-(5-((1R,2S)-2-fluorocyclopropyl)-1,2,4-oxadiazol-3-yl)-2-methylphenyl)imidazo[1,2-a]pyridine-3-carboxamide Form HB characterized by having a powder X-ray diffractogram comprising reflections at 2-Theta angles of $(6.7 \pm 0.2)^\circ$, $(13.6 \pm 0.2)^\circ$, and $(18.0 \pm 0.2)^\circ$, when measured at a temperature in the range of from 20 to 30 °C with Cu-Kalpha radiation having a wavelength of 0.15406 nm.