CLAIMS

1. A polymorph of varoglutamstat hydrochloride which is characterized by X-ray powder diffraction peaks (2[Theta]) selected from one or more of the following: 9.5±0.2°, and 24.8±0.2°.

2. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, which is characterized by X-ray powder diffraction peaks (2[Theta]) selected from one or more of the following: 9.5±0.2°, 21.3±0.2°, 22.6±0.2°, and 24.8±0.2°.

3. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, which is characterized by X-ray powder diffraction peaks (2[Theta]) selected from one or more of the following: 5.8±0.2°, 9.5±0.2°, 16.9±0.2°, 17.2±0.2°, 18.9±0.2°, 20.7±0.2°, 21.3±0.2°, 21.7±0.2°, 22.6±0.2°, and 24.8±0.2°.

4. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, which is characterized by X-ray powder diffraction peaks (2[Theta]) selected from one or more of the following: 5.8±0.2°, 9.5±0.2°, 11.3±0.2°, 12.4±0.2°, 15.8±0.2°, 16.9±0.2°, 17.2±0.2°, 18.9±0.2°, 20.2±0.2°, 20.7±0.2°, 21.3±0.2°, 21.7±0.2°, 22.6±0.2°, 23.8±0.2°, 24.8±0.2°, 26.3±0.2°, 27.2±0.2°, 28.3±0.2°, 28.8±0.2°, 29.4±0.2°, 30.1±0.2°, 31.2±0.2° and 33.8±0.2°.

5. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by an X-ray diffraction spectrum as shown in Figure 19.

6. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by a differential scanning calorimetry (DSC) thermogram as shown in Figure 20.

7. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by an DSC endotherm with an onset temperature of 243°C and with a peak at 251°C.

8. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by a dynamic vapor sorption (DVS) curve as shown in Figure 22.

9. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by a thermogravimetric analysis (TGA) thermogram as shown in Figure 21.

10. The polymorph of varoglutamstat hydrochloride as claimed in claim 9, characterized by one mass loss of 3.0 % with onset/endset temperatures of 190/215°C before the main thermal decomposition of said varoglutamstat hydrochloride.

11. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by a ^{1}H-NMR spectrum as shown in Figure 23.

12. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, wherein said polymorph is substantially free of amorphous material.

13. The polymorph of varoglutamstat hydrochloride as claimed in claim 1, characterized by an achiral purity of >95%, or >96%, or >97%, or >98%, or >99%, or >99.5%, or >99.8%, wherein achiral purity is determined by ^{1}H-NMR analysis.

14. A hydrochloride salt of varoglutamstat ((S)-1-(1H-benzo[d]imidazol-5-yl)-5-(4-propoxyphenyl)imidazolidin-2-one) consisting of a polymorph as claimed in claim 1.

15. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein said hydrochloride salt of varoglutamstat is non-hygroscopic.

16. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein said hydrochloride salt of varoglutamstat shows a water uptake < 6.0 % at 95% RH.

17. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein the TGA profile of said hydrochloride salt of varoglutamstat shows a mass loss < 9.20% corresponding to <2 water molecules per mol or any other solvate related substance.

18. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein said hydrochloride salt of varoglutamstat shows a degree of crystallinity of > 50 %, when calculated with formula I:

% Crystallinity = 100 x A / (A + B – C) (Formula I)

wherein

A is the sum of the net areas of all the peaks arising from the diffraction of the crystalline fraction of the sample;

B is the area under the diffractogram generated by the sample itself (excluding area A); and

C is the area of the background noise (due to air scattering, fluorescence, equipment, etc.) which is measured by recording the diffractograms of the (empty) sample holder that was used for recording the diffractograms of the tested samples.

19. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein crystals of said hydrochloride salt of varoglutamstat comprise needles as shown in Figure 18.

20. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein said hydrochloride salt of varoglutamstat has a solubility in water at 20°C of ≥ 0.10 M, or ≥ 0.11 M, or ≥ 0.12 M, or ≥ 0.13 M or ≥ 0.14 M.

21. The hydrochloride salt of varoglutamstat as claimed in claim 14, wherein crystals of said hydrochloride salt of varoglutamstat is substantially free of isopropyl chloride.

22. A process for preparing a hydrochloride salt of varoglutamstat as claimed in claim 14, said process comprising dissolving varoglutamstat free base in a solvent mixture comprising a polar aprotic water-mixable organic solvent and water, adding a solution comprising HCl, and harvesting varoglutamstat hydrochloride crystals.

23. The process as claimed in claim 22, comprising:

i. Dissolving varoglutamstat free base in a polar aprotic water-mixable organic solvent;

ii. Adding water to the solvent of step i to produce an organic solvent - water mixture;

iii. Adding a solution comprising aqueous HCl to the organic solvent - water mixture of step ii;

iv. Optionally adding seed crystals to the solution of step iii;

v. Ripening the resulting mixture of step iii and/or step iv for a time period sufficient to form a ripened mixture of varoglutamstat hydrochloride crystals;

vi. Adding to the ripened mixture polar aprotic water-mixable organic solvent to obtain a suspension of varoglutamstat hydrochloride crystals;

vii. Cooling of the suspension obtained in step vi; and

viii. Harvesting the varoglutamstat hydrochloride crystals.

24. The process as claimed in claim 22, said process comprising the steps of:

i. Dissolving 1 eq. varoglutamstat free base in 5 vol. acetone and heating resulting solution to 45±5°C;

ii. Adding to the resulting solution in step i water in an amount of 221 mg water per mmol free base while maintaining the solution at 45±5°C;

iii. Adding a solution comprising 3 vol. acetone and 0.95 eq of aqueous HCl (32-37% w/w) to the solution produced in step ii;

iv. Adding seed crystals to the solution of step iii;

v. Incubating the resulting suspension of step iii and/or step iv for a time period sufficient to form a suspension of varoglutamstat hydrochloride crystals;

vi. Adding 16 vol. acetone to said suspension while keeping temperature of the suspension at 45±5°C;

vii. Cooling of the suspension obtained in step vi to 20±5°C;

viii. Stirring the suspension of step vii;

ix. Harvesting varoglutamstat hydrochloride crystals from the suspension of step vii by filtration;

x. Rinsing harvested varoglutamstat hydrochloride crystals obtained by filtration in step ix with an acetone / water mixture of 48 : 1.6 v/v to obtain rinsed varoglutamstat hydrochloride crystals;

xi. Rinsing the rinsed crystals obtained in step x twice with pure acetone; and

xii. Drying the crystals rinsed twice with pure acetone in step xi.

25. A pharmaceutical composition comprising a therapeutically effective dose of the hydrochloride salt of varoglutamstat as claimed in claim 14, together with a pharmaceutically acceptable carrier, diluent, or excipient therefor.

26. The pharmaceutical composition as claimed in claim 25, additionally comprising at least one compound selected from the group consisting of neuroprotectants, antiparkinsonian drugs, amyloid protein deposition inhibitors, beta amyloid synthesis inhibitors, antidepressants, anxiolytic drugs, antipsychotic drugs, anti-multiple sclerosis drugs and monoclonal antibodies.

27. Use of the polymorph of varoglutamstat hydrochloride as claimed in claim 1 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of neurodegenerative diseases, inflammatory diseases, infectious diseases, proliferative diseases, tumours, and kidney diseases, wherein the medicament is to be administered to a subject in need thereof..

28. The process as claimed in claim 23, wherein said polar aprotic water-mixable organic solvent is acetone.

29. The process as claimed in claim 22 wherein the polar aprotic water-mixable organic solvent is acetone.

30. A pharmaceutical composition comprising a therapeutically effective dose of the polymorph as claimed in claim 1, together with a pharmaceutically acceptable carrier, diluent, or excipient therefor.