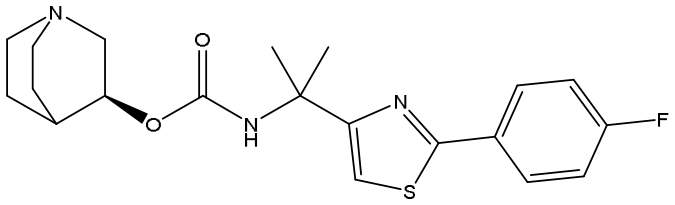
CLAIMS

We claim:

1. A process for the manufacture of an oral pharmaceutical composition comprising venglustat, (S)-quinuclidin-3-yl 2-(2-(4-fluorophenyl)thiazol-4-yl)propan-2-ylcarbamate:



in free base or pharmaceutically acceptable salt form, wherein the process comprises the steps of:

(a) sieving each ingredient;

(b) combining venglustat, in free base or pharmaceutically acceptable salt form, with a diluent/filler, and optionally with a lubricant, a glidant, any colors or flavors, or any other excipients, or a combination thereof;

(c) blending and/or milling and/or granulating the resulting the mixture;

(d) optionally screening the resulting mixture;

(e) adding at least one other diluent or carrier to the mixture, such as additional diluent/filler, a disintegrant, a binder, a lubricant, or any other excipient, or a combination thereof, wherein, if a lubricant is not combined with the venglustat and the diluent/filler in step (b), a lubricant is added to the mixture;

(f) blending and/or milling and/or granulating the resulting mixture;

(g) optionally screening the resulting mixture;

(h) adding a lubricant and any additional excipients;

(i) blending and/or milling the resulting mixture;

(j) optionally granulating the resulting mixture;

(k) optionally screening the resulting mixture;

(l) encapsulating the resulting material; or compressing the resulting material to form a tablet;

(m) optionally applying one or more coatings to the capsule, tablet, or other dosage form; and

(n) optionally packaging the resulting finished dosage form.

2. The process according to claim 1, wherein the venglustat is venglustat malate.

3. The process according to claim 1 or claim 2, wherein steps (i), (j), and/or (k) are repeated for additional excipients added in step (h) before proceeding to steps (l), (m), or (n).

4. The process according to any one of claims 1 to 3, wherein a lubricant is combined with the venglustat and the diluent/filler in step (b).

5. The process according to any one of claims 1 to 4, wherein the composition is a solid tablet, and wherein sodium stearyl fumarate is added as a first lubricant in combining step (b).

6. The process according to any one of claims 1 to 5, wherein the composition is a solid tablet, and wherein magnesium stearate is added as a second lubricant which is added as the final excipient added before final mixing and compression to form the tablet.

7. The process according to any one of claims 1 to 6, wherein the diluent/filler is mannitol, and the disintegrant is crospovidone, and the binder is hydroxypropyl cellulose, and the lubricant is sodium stearyl fumarate and/or magnesium stearate, and the glidant is silica.

8. The process according to any one of claims 1 to 3, wherein the process comprises the following steps:

(a) sieving one or more ingredients, for example, all ingredients, or only some ingredients (e.g., sieving half of the amount of microcrystalline cellulose, and/or silica), and lubricant (magnesium stearate and/or sodium stearyl fumarate));
(b) combining venglustat malate with microcrystalline cellulose (a first portion), sucralose (if any), flavor (if any), and croscarmellose sodium, optionally wherein these ingredients are not previously sieved;
(c) blending and/or milling and/or granulating the resulting mixture;
(d) optionally sieving the resulting mixture;
(e) adding microcrystalline cellulose (second portion), silica, and a first portion of lubricant (magnesium stearate and/or sodium stearyl fumarate) to the mixture

from step (c), optionally wherein these added ingredients are previously sieved from step (a);

(f) blending and/or milling and/or granulating the resulting mixture;

(h) sieving the remaining portion of lubricant (magnesium stearate and/or sodium stearyl fumarate), and/or adding it to the mixture from step (f);

(i-j) blending and/or milling and/or granulating the resulting mixture;

(l) filling the resulting material into hard capsules; and

(n) optionally packaging the resulting finished dosage form.

9. The process according to claim 8, wherein first and remaining portions of magnesium stearate lubricant are added in steps (e) and (h).

10. The process according to claim 9, wherein the first portion comprises 15-50% by weight, or 20-30% by weight, of the total magnesium stearate lubricant added, and wherein the remaining portion comprises 50-85% by weight, or 70-80% by weight, of the total magnesium stearate lubricant added.

11. The process according to any one of claims 1 to 7, wherein the process comprises the following steps:

(a) sieving each of mannitol (a first portion thereof), silica, venglustat malate, sucralose (if any), flavor, and sodium stearyl fumarate;

(b) combining the venglustat malate with the sieved mannitol, silica, sucralose (if any), flavor, and sodium stearyl fumarate, optionally wherein in each ingredient is sieved sequentially into a common container to combine the ingredients;

(c) blending and/or milling and/or granulating the resulting mixture;

(e) sieving mannitol (second portion), low-substituted hydroxypropyl cellulose, and crospovidone, and adding these sieved ingredients to the mixture from step (c);

(f) blending and/or milling and/or granulating the resulting mixture;

(h) sieving magnesium stearate and adding it to the mixture from step (f);

(i-j) blending and/or milling and/or granulating the resulting mixture;

(l) compressing the resulting material to form a tablet; and

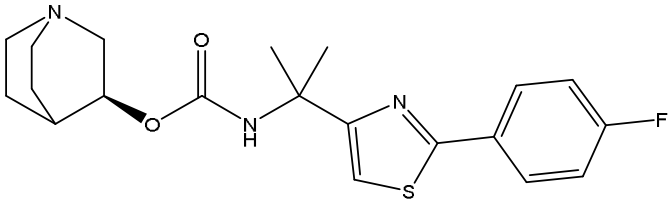
(n) optionally packaging the resulting finished dosage form.

12. The process according to claim 11, wherein sodium stearyl fumarate is combined in step (b) in an amount to provide 2-3% by weight sodium stearyl fumarate in the tablet.

13. The process according to claim 11 or claim 12, wherein magnesium stearate is added in step (h) in an amount to provide from 0.1-1% by weight magnesium stearate in the tablet.

14. A composition prepared, or preparable, by the process as defined in any one of the preceding claims.

15. An oral pharmaceutical composition comprising venglustat, (S)-quinuclidin-3-yl 2-(2-(4-fluorophenyl)thiazol-4-yl)propan-2-ylcarbamate:



in free base or pharmaceutically acceptable salt form, a diluent/filler, and a lubricant.

16. The composition of claim 15, wherein the composition further comprises one or more additional pharmaceutically acceptable excipients selected from diluent/filler, binder, disintegrant, lubricant, a glidant, sweetener or flavor, and dye or colorant.

17. The composition of claim 15 or claim 16, wherein the venglustat is venglustat malate.

18. The composition of any one of claims 15 to 17, wherein the composition is in a finished dosage form selected from a capsule, or a tablet selected from a chewable tablet, an orally-disintegrating tablet, a dispersible tablet, or a classic tablet or caplet; optionally wherein said finished dosage form comprises from about 2 to about 30 mg of venglustat (measured as the equivalent amount of free base).

19. The composition of claim 18, wherein the finished dosage form is a capsule, comprising or consisting of (a) venglustat, (b) the diluent/filler cellulose (e.g., microcrystalline cellulose), (c)

the lubricant magnesium stearate, (d) the disintegrant croscarmellose sodium, (e) the glidant silica (e.g., colloidal and/or anhydrous silica), (f) flavor, sweetener and/or color, and (g) a capsule shell.

20. The composition of claim 18, wherein the finished dosage form is a tablet, comprising or consisting of (a) venglustat, (b) the diluent/filler mannitol, (c) the lubricants magnesium stearate and sodium stearyl fumarate, (d) the disintegrant crospovidone, (e) the binder hydroxypropyl cellulose (e.g., low-substituted hydroxypropyl cellulose), (f) the glidant silica (e.g., colloidal and/or anhydrous silica), and (g) flavor, sweetener, and/or color.

21. The composition of claim 19 or claim 20, wherein the composition comprises (a) from 3% to 20% (e.g., from 7.5% to 12.5%, or from 13-20%) by weight of venglustat, measured as the free base equivalent; (b) from 60-90% (e.g., from 60-70%) by weight of diluent(s)/filler(s); (c) from 0.5-6% (e.g., from 2-4%) by weight of lubricant(s); (d) from 2-15% (e.g., from 6-10%) by weight of disintegrant(s); (e) from 1-12% (e.g., from 2-6%) by weight of binder(s); (f) from 0-5% (e.g., from 0.5-1.5%) by weight of glidant(s); and (g) from 0-2% by weight of flavor(s), 0-2% by weight of sweetener(s), and/or 0-2% by weight of color(s).

22. The composition of claim 20, wherein the composition comprises or consists of (a) venglustat malate in an amount from about 9-11% by weight of venglustat free base equivalent; (b) from 65 to 70% by weight of mannitol; (c) from 2-3% by weight of sodium stearyl fumarate, and 0.1-1% magnesium stearate; (d) from 7-9% by weight of crospovidone; (e) from 4-6% by weight of low-substituted hydroxypropyl cellulose; (f) from 0.5-1.5% by weight of anhydrous colloidal silica; (g) from 0.5-3% by weight of flavor; and (h) from 0-2% by weight of sweetener.

23. The composition of any one of claims 14 to 22, wherein the composition is formulated for immediate-release.

24. The composition of any one of claims 14 to 23, wherein the composition provides at least 80% dissolution within 15 minutes (e.g., using FDA and/or EMEA immediate-release solid oral dosage form testing guidelines), such as in pH 1.2 (HCl), pH 4.5 (acetate buffer), or pH 6.8 (phosphate buffer) dissolution medium, for example 85-100% dissolution.

25. The composition of any one of claims 14 to 18, and 20 to 24, wherein the composition is a chewable tablet having a chewing difficulty index selected from less than 0.6 Nm, or less than 0.5 Nm, or less than 0.4 Nm, or less than 0.2 Nm.

26. The composition of any one of claims 14 to 25 for use in the treatment or prevention of a disease or disorder susceptible to treatment by GCS inhibition in a patient in need thereof.

27. The use of a composition of any one of claims 14 to 25 in the manufacture of a medicament for the treatment or prevention of a disease or disorder susceptible to treatment by GCS inhibition in a patient in need thereof.