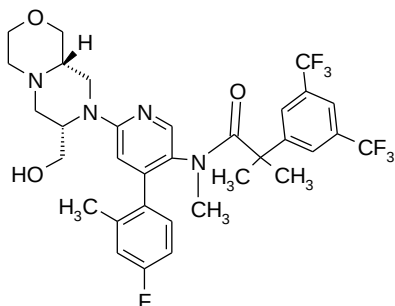


CLAIMS

1. A ~~soft gelatin capsule pharmaceutical~~ formulation, comprising:

(a) 2-[3,5-Bis(trifluoromethyl)phenyl]-N-{4-(4-fluoro-2-methylphenyl)-6-

[(7S,9aS)-7-(hydroxymethyl)hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl]-3-pyridinyl]-N,2-dimethylpropanamide (Compound A):



(Compound A)

or a pharmaceutically acceptable salt thereof; and

(b) at least one solubilizer selected from caprylocaproyl polyoxyl-8 glycerides, glycerol monocaprylocaprate, polyoxyl 35 castor oil, polysorbate 80, or mixtures thereof; and

(c) at least one antioxidant selected from dl-alpha tocopherol, butylated hydroxytoluene, and butylated hydroxyanisole, or mixtures thereof.

2. The ~~pharmaceutical~~ formulation of claim 1, wherein Compound A is in a crystalline form.

3. The ~~pharmaceutical~~ formulation of claims 1 ~~or 2~~, wherein Compound A is a crystalline form characterized by an XRPD pattern having a 2 theta angle peak at 4.3±0.1 degree, 7.9±0.1 degree, 9.8±0.1 degree, 10.7±0.1 degree, 10.8±0.1 degree, 13.3±0.1 degree, 14.0±0.1 degree, and 15.1±0.1 degree, which correspond respectively to d-spacing at 20.4, 11.1, 9.0, 8.3, 8.2, 6.6, 6.3 and 5.9 Angstroms (A) in anhydrous crystalline Form 1.

4. ~~The pharmaceutical formulation of any one of claims 1-3, further comprising an antioxidant.~~

5. ~~The pharmaceutical formulation of any one of claims 1-4, further comprising (d) at least one an emulsifier selected from glyceryl monooleate, Miglyol 812, or a mixture thereof.~~

6. ~~The pharmaceutical formulation of any one of claims 1-5, further comprising one or more additional therapeutic agents.~~

7. ~~The pharmaceutical formulation of any one of claims 1 or 4-6, being of a liquid oral formulation.~~

8. ~~The pharmaceutical formulation of any one of claims 1-7, being of a soft gelatin capsule.~~

9.6. ~~The pharmaceutical formulation of any one claims 1-8, wherein concentration of Compound A is present in the pharmaceutical formulation at a concentration ranges from 0.8 % w/w to 15% w/w.~~

5 10.7. ~~The pharmaceutical formulation of any one of claims 1-9, wherein the amount of Compound A is present in the pharmaceutical formulation ranges in an amount from 10 mg to 80 mg.~~

10 11.8. ~~The pharmaceutical formulation of any one claims 1-10, wherein the at least one solubilizer is selected from Caprylocaproyl polyoxyl-8 glycerides (Labrasol ALF), Glycerol Monocaprylocaprate-monocaprylocaprate (Capmul-MCM), caprylocaproyl polyoxyl-8 glycerides, Polyoxyl-35 castor oil (Kolliphor-EL), or polysorbate 80 (Tween-80), or mixtures thereof.~~

15 12. ~~The pharmaceutical formulation of any one of claims 1-10, wherein the solubilizer is a mixture of Glycerol Monocaprylocaprate (Capmul-MCM), Caprylocaproyl polyoxyl-8 glycerides (Labrasol ALF), and Polysorbate 80 (Tween-80), wherein the concentration of the Glycerol Monocaprylocaprate (Capmul-MCM) ranges from 30% w/w to 40% w/w, the concentration of Caprylocaproyl polyoxyl-8 glycerides (Labrasol ALF) ranges from 9% w/w to 10% w/w, the concentration of the Polysorbate 80 (Tween-80) ranges from 9% w/w to 10% w/w.~~

25 13.9. ~~The pharmaceutical formulation of any one claims 5-12, wherein the at least one emulsifier is Glyceryl glyceryl Monooleate monooleate (Peceol).~~

14. ~~The pharmaceutical formulation of any one claims 4-13, wherein the antioxidant is selected from DL-Alpha-tocopherol (Vitamin E), butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA), and mixtures thereof.~~

30 15.10. ~~The pharmaceutical formulation of claim 14, wherein the at least one antioxidant is DLdl-Alpha-alpha tocopherol (Vitamin E) at a concentration ranging from 0.05% w/w to 1.5% w/w.~~

35 16.11. ~~The pharmaceutical formulation of any one of claims 1-15, comprising~~
~~(a) Compound A;~~
~~(b1) Glycerol-glycerol Monocaprylocaprate-monocaprylocaprate; (Capmul-MCM);~~
~~(b2) caprylocaproyl polyoxyl-8 glycerides;~~
~~(b3) Polysorbate 80 (Tween-80); and~~
~~(c), Glyceryl Monooleate (Peceol), and DLdl-alpha tocopherol (Vitamin E).~~

40 17.12. ~~The pharmaceutical formulation of any one of claims 1-15, comprising~~
~~(a) Compound A;~~
~~(b1) Glycerol Monocaprylocaprate (Capmul-MCM);~~
~~(b2) Caprylocaproyl polyoxyl-8 glycerides (Labrasol ALF);~~
45 ~~(b3) polysorbate 80 (Tween-80);~~
~~(c) dl-alpha tocopherol; and~~

~~(d) Glyceryl Monooleate (Pecceol), and DL-alpha tocopherol (Vitamin E).~~

~~18. The pharmaceutical formulation of claim 17, comprising:~~

~~13. (a) wherein Compound A is present in the formulation at a concentration ranging from about 1% w/w to about 10% w/w or from 5% w/w to 10% w/w;~~

~~(b1) Glycerol Monocaprylocaprate (MCM) presented at a concentration ranging from 30% w/w to 40% w/w;~~

~~(b2) Caprylocaproyl polyoxyl-8 glycerides (Labrasol ALF) presented at a concentration ranging from 7% w/w to 13% w/w;~~

~~(b3) Polysorbate 80 (Tween 80) presented at a concentration from 7% w/w to 13% w/w;~~

~~(c) Glyceryl Monooleate (Pecceol) presented at a concentration ranging from about 33% w/w to 43% w/w; and~~

~~(d) DL-Alpha tocopherol (Vitamin E) presented at a concentration ranging from 0.05% w/w to 1.5% w/w or ranging from 0.5% w/v to 1.0% w/v.~~

~~14. The formulation of claim 8, wherein the glycerol monocaprylocaprate is present in the formulation at a concentration ranging from 20% w/w to 65% w/w.~~

~~15. The formulation of claim 8, wherein the caprylocaproyl polyoxyl-8 glycerides is present in the formulation at a concentration ranging from 7% w/w to 13% w/w.~~

~~16. The formulation of claim 8, wherein the polysorbate 80 is present in the formulation at a concentration from 7% w/w to 13% w/w.~~

~~17. The formulation of claim 9, wherein the glyceryl monooleate is present in the formulation at a concentration ranging from 15% w/w to 60% w/w.~~

~~18. The formulation of claim 10, wherein dl-alpha-tocopherol is present in the formulation at a concentration ranging from 0.05% w/w to 1.5% w/w.~~

~~19. A soft gelatin capsule formulation comprising:~~

~~(a) Compound A present at a concentration ranging from 5% w/w to 10% w/w;~~

~~(b1) glycerol monocaprylocaprate present at a concentration ranging from 20% w/w to 65% w/w;~~

~~(b2) caprylocaproyl polyoxyl-8 glycerides present at a concentration ranging from 7% w/w to 13% w/w;~~

~~(b3) polysorbate 80 present at a concentration from 7% w/w to 13% w/w;~~

~~(c) dl-alpha-tocopherol present at a concentration ranging from 0.5% w/w to 1% w/w; and~~

~~(d) glyceryl monooleate.~~

~~20. The formulation of claim 19, wherein the glyceryl monooleate is present in the formulation at a concentration ranging from 15% w/w to 60% w/w.~~

21. The formulation of claim 19, being prepared by a method comprising adding Compound A to a mixture comprising 15% w/w to 60% w/w glyceryl monooleate, glycerol monocaprylocaprate, caprylocaproyl polyoxyl-8 glycerides, polysorbate 80, or dl-alpha-tocopherol.

22. A soft gelatin capsule formulation comprising:

(a) Compound A present at a concentration ranging from 1% w/w to 10% w/w;

(b1) glycerol monocaprylocaprate present at a concentration ranging from 30% w/w to 40% w/w;

(b2) caprylocaproyl polyoxyl-8 glycerides present at a concentration ranging from 7% w/w to 13% w/w;

(b3) polysorbate 80 present at a concentration from 7% w/w to 13% w/w;

(c) dl-alpha-tocopherol present at a concentration ranging from 0.5% w/w to 1% w/w; and

(d) glyceryl monooleate.

23. The formulation of claim 22, wherein glyceryl monooleate is present in the formulation at a concentration ranging from 33% w/w to 43% w/w.

24. The formulation of claim 22, being prepared by a method comprising adding Compound A to a mixture comprising 33% w/w to 43% w/w glyceryl monooleate, glycerol monocaprylocaprate, caprylocaproyl polyoxyl-8 glycerides, polysorbate 80, and dl-alpha-tocopherol.

25. Use of the soft gelatin capsule formulation of any one of claims 1-24, in the manufacture of a medicament for the treatment or prevention of a sex hormone dependent disease, or in the treatment or prevention of a condition, wherein the condition is a symptom associated with the perimenopause, the menopause, or the post menopause are selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances and night-time awakenings, anxiety and depression, urinary symptoms of urgency and dysuria; or wherein the condition is a symptom associated with andropause selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances and night-time awakenings, anxiety and depression, urinary symptoms of urgency, dysuria, vasomotor symptoms associated with menopause or vasomotor symptoms caused by therapy with aromatase inhibitors or selective estrogen receptor modulators.

26. The use of claim 25, wherein the sex-hormone dependent disease is selected from endometriosis, uterine fibroid tumor, heavy menstrual bleeding, polycystic ovary syndrome (PCOS) and vasomotor symptoms.

27. The use of claim 26, wherein the sex-hormone dependent disease is vasomotor symptoms.

19. — ~~The pharmaceutical formulation of any one of claims 1-18, for use in the treatment or prevention of a sex hormone dependent disease, or in the treatment or prevention of a condition, wherein the condition is a symptom associated with the perimenopause, the menopause, or the post menopause. selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances and night-time awakenings, anxiety and depression, urinary symptoms of urgency and dysuria; or wherein the condition is a symptom associated with andropause selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances and night-time awakenings, anxiety and depression, urinary symptoms of urgency and dysuria.~~

20. — ~~The pharmaceutical formulation for use of claim 19, wherein the sex-hormone dependent disease is selected from endometriosis, uterine fibrosis, heavy menstrual bleeding, polycystic ovary syndrome (PCOS) and hot flushes.~~

21. — ~~The pharmaceutical formulation for use of claim 19, wherein the sex-hormone dependent disease is hot flushes.~~

22. — ~~Compound A or pharmaceutically acceptable salts thereof for use in the treatment or prevention of a condition, wherein the condition is a symptom of the perimenopause, the menopause, or the post menopause selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances and night-time awakenings, anxiety and depression, urinary symptoms of urgency and dysuria; or a symptom associated with the andropause selected from a pathological gain of excess body fat and/or excess body weight, insomnia, sleep disturbances, night-time awakenings, anxiety and depression, urinary symptoms of urgency and dysuria.~~

23. — ~~A method for preparing the pharmaceutical formulations according to claims 1-18 by mixing Compound A or a pharmaceutically acceptable salts thereof with at least of one excipient.~~

24. — ~~The method of claim 23, wherein Compound A is in anhydrous crystalline Form 1.~~

25. — ~~A method for producing a soft gelatin capsule comprising the steps of providing a capsule shell, mixing a formulation comprising Compound A or pharmaceutically acceptable salts thereof and at least one excipient, and incorporating the formulation into the capsule shell.~~