CLAIMS

1. Use of an effective amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, for the manufacture of a dosage form for treating or preventing a disease or disorder, wherein said disease or disorder is selected from the group consisting of a chronic granulomatous disorder, a polycystic ovary syndrome, a thyroid carcinoma, a thyroid autoimmune disorder, a pituitary adenoma, atherosclerosis, hypertension, a skin disease, an inflammation and autoimmune disease, an inflammatory respiratory disease, and a mitochondrial disease.

2. Use of an effective amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, for the manufacture of a dosage form for treating or preventing of a nonalcoholic fatty liver disease (NAFLD) or a nonalcoholic steatohepatitis (NASH), wherein said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is metabolized after oral administration to the patient providing plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient of 30 µg.h/mL to 300 µg.h/mL measured after at least 5 days of administering said dosage form to the patient per day.

3. Use of an effective amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, for the manufacture of a dosage form for treating or preventing a central nervous system disorder, wherein said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is metabolized after oral administration to the patient providing plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient of 100 µg.h/mL to 300 µg.h/mL measured after at least 5 days of administering said dosage form to the patient per day.

4. The use of claim 3, wherein the plasma concentration is 100 µg.h/mL to 200 µg.h/mL or 150 µg.h/mL to 250 µg.h/mL.

5. The use of claim 3 or claim 4, wherein the central nervous system disorder is selected from the group consisting of a neurodegenerative disease, a cerebrovascular disease, seizure, epilepsy, a viral disease, a neuroinflammatory disease, a brain tumour, a traumatic brain injury, and a rare metabolic disease.

6. The use according to claim 5, wherein the neurodegenerative disease is selected from the group consisting of leukodystrophy, amyotrophic lateral sclerosis (ALS), Parkinson's disease, multiple sclerosis, Alzheimer's disease, Huntington's chorea, degenerative ataxia, multiple system atrophy, a motor neuron disease, neuromyelitis optica, NBIA (neurodegeneration and brain iron accumulation disorders), and neuromyopathy.

7. The use of claim 6, wherein the leukodystrophy is adrenoleukodystrophy (ALD or X-ALD); the degenerative ataxia is Friedreich's ataxia; and the motor neuron disease is selected from the group consisting of progressive bulbar palsy, pseudobulbar palsy, primary lateral sclerosis (PLS), progressive muscular atrophy, spinal muscular atrophy (SMA), post-polio syndrome (PPS)-Marie-Tooth disease, Guillan-Barré syndrome, and adrenomyeloneuropathy (AMN).

8. The use of claim 5, wherein the central nervous system disorder is a cerebrovascular disease selected from the group consisting of global or local ischemia, intracerebral haemorrhage, stroke, and vascular dementia; or the central nervous system disorder is a viral disease selected from the group consisting of meningitis, encephalitis, rabies, measles, mumps, poliomyelitis, herpes simplex, and varicella zoster; or the central nervous system disorder is a rare metabolic disease selected from the group consisting of organic acidemias, fatty acid disorders and genetic mitochondrial disorders.

9. The use of any one of claims 1-8, wherein said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione or a pharmaceutically acceptable salt is administered at a daily dose of from 10 mg to 500 mg or from 50 mg to 500 mg.

10. The use of any one of claims 3-9, wherein a detectable amount of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is found in the central nervous system (CNS) of the subject after administration.

11. The use of claim 10, wherein said 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is found in the CNS of the subject at an exposure of at least about 100 µg.h/mL after 1 hour after oral administration of a dose of said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, wherein said dose is from 10 mg to 500 mg.

12. The use of claims 1 or 9, wherein the mitochondrial disease is a primary mitochondrial disorder selected from the group consisting of Rett syndrome, Alper's disease; Leber's hereditary optic neuropathy (LHON); Kearns-Sayre syndrome (KSS); Leigh's syndrome; Leigh-like syndrome; maternally inherited Leigh syndrome (MILS); mitochondrial depletion syndrome (MDS); mitochondrial DNA depletion syndrome (MDDS); mitochondrial encephalomyopathy; mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE); neuropathy, ataxia, and retinitis pigmentosa (NARP); Pearson syndrome; chronic progressive external opthalmoplegia (CPEO); dominant optic atrophy (DOA); autosomal dominant optic atrophy (ADOA); mitochondrial myopathy; cardiomyopathy; mitochondrial encephalopathy; myoclonic epilepsy; maternally inherited diabetes and deafness (MIDD); ataxia neuropathy spectrum; 3-methylglutaconic aciduria; sensoneural deafness; neuroradiological findings of Leigh-like syndrome (MEGDEL); SURF1 (COX definient Leigh syndrome due to complex IV surfeit protein deficiency); oxidative phosphorylation disorders; Berth syndrome; lethal infantile cardiomyopathy (LIC); pyruvate carboxylase deficiency; pyruvate dehydrogenase deficiency; POLG mutation; isolated or combined OXPHOS deficiencies with so far unsolved genetic defect including disturbed pyruvate oxidation and ATP plus PCr production rates; POLG2 mutation; carnitine-acyl-cartinine deficiency; carnitine deficiency; creatinine deficiency syndromes; Co-Enzyme Q10 deficiency; Complex I deficiency; Complex II deficiency; Complex III deficiency; Complex IV deficiency; Complex V deficiency; lactic acidosis; leukoencephalopathy with

brain stem and spinal cord involvement and lactate elevation (LBSL); Luft disease; carnitine palmitoyltransferase (CPT I or CPT II) deficiency; short-chain acyl-CoA dehydrogenase deficiency (SCAD); short-chain 3-hydroxyacetyl-CoA dehydrogenase deficiency (SCHAD); medium-chain acyl-CoA dehydrogenase deficiency (MCAD); multiple acyl-CoA dehydrogenase deficiency (MADD); long-chain acyl-CoA dehydrogenase deficiency (LCAD); very long-chain acyl-CoA dehydrogenase deficiency (VLCAD); trifunctional protein (TFP) deficiency; and glutaric aciduria Type II.

13. The use of claim 12, wherein the mitochondrial disease is selected from the group consisting of Rett syndrome; dominant optic atrophy (DOA); autosomal dominant optic atrophy (ADOA); Complex I deficiency; Leber hereditary optic neuropathy (LHON); Kearns-Sayre syndrome (KSS); Leigh's syndrome; mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE); neuropathy, ataxia, and retinitis pigmentosa (NARP); Pearson syndrome; and chronic progressive external opthalmoplegia (CPEO).

14. The use of claims 1 or 9, wherein the mitochondrial disease is a secondary mitochondrial disorder selected from the group consisting of Duchenne muscular dystrophy (DMD); Becker muscular dystrophy (BMD); myotonic dystrophy (BMD); congenital myopathies; glycogen storage disorders; spinal-bulbar muscular atrophy (SBMA); argininosuccinic aciduria; autism spectrum disorder (ASD); autoimmune diseases of the skin (such as pemphigus vulgaris and lupus); methylmalonic and propionic acidurias; disorders or purine and/or pyrimidine synthesis; facioscapulohumeral muscular dystrophy (FSHD); congenital muscular dystrophies; collagen VI muscular dystrophies (e.g., Ullrich congenital muscular dystrophy, Bethlem myopathy, oculopharyngeal distal, and Emery-Dreifuss); DiGeorge syndrome; and neuromuscular disorders (such as limb-girdle muscular dystrophy, inflammatory myopathies, Charcot Marie Tooth (CMT) neuropathy, and drug-induced peripheral neuropathies).

15. The use of any one of claims 1, 9, or 12-14, wherein said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is metabolized after oral

administration to the patient providing plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient of 30 µg.h/mL to 300 µg.h/mL measured after at least 5 days of administering said dosage form to the patient per day.

16. The use of claim 2 or 15, wherein the plasma concentration is 30 µg.h/mL to 100 µg.h/mL or 100 µg.h/mL to 300 µg.h/mL.

17. The use of any one of claims 1 to 16, wherein the patient is also administered another therapeutic agent.

18. The use of any one of claims 1 to 17, wherein no more than 1 % of the total number of hydrogen atoms per mole of said 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione are in the form of the ^{2}H isotope.

19. Use of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treatment of a disease or disorder in a patient in need thereof, wherein 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is metabolized to 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient after oral administration, and:

(a) the steady-state area under the curve (AUC_{ss}) of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient is 34 µg·h/mL to 300 µg·h/mL;

(b) the minimum steady-state plasma drug concentration ($C_{min\ ss}$) of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient is 55 to 9126 ng/mL; or

(c) the AUC_{ss} of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient is 34 µg·h/mL to 300 µg·h/mL, and the $C_{min\ ss}$ of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient is 55 to 9126 ng/mL; and

the AUC_{ss} of (a), the $C_{min\ ss}$ of (b), or the AUC_{ss} and $C_{min\ ss}$ of (c) is measured after at least five days of orally administering the medicament comprising 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, to the patient per day.

20. The use of claim 19, wherein the AUC_{ss} of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is 100 µg·h/mL to 300 µg·h/mL, or 150 µg.h/mL to 250 µg.h/mL, or 175 µg.h/mL to 225 µg.h/mL, or about 200 µg.h/mL, or 30 µg.h/mL to 100 µg.h/mL, or 50 µg.h/mL to 200 µg.h/mL.

21. The use of claims 19 or 20, wherein the $C_{min\ ss}$ of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione is 2306 to 9126 ng/mL, or 5000 to 6500 ng/mL, or 5500 to 6000 ng/mL, or about 5716 ng/mL.

22. The use of any one of claims 19-21, wherein the AUC_{ss}, $C_{min\ ss}$, or AUC_{ss} and $C_{min\ ss}$ is measured after at least seven days, or after at least ten days, or after at least fourteen days.

23. The use of any one of claims 19-22, wherein 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione hydrochloride is administered to the patient in need thereof.

24. The use of claim 23, wherein the 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione hydrochloride is administered to the patient as a suspension comprising 5-15 mg of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione hydrochloride per mL.

25. The use of any one of claims 19-24, wherein the disease or disorder is selected from the group consisting of central nervous system disease or disorder, mitochondrial disease, nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver disease (NAFLD), chronic granulomatous disorder, a polycystic ovary syndrome, a thyroid carcinoma, a thyroid

autoimmune disorder, a pituitary adenoma, atherosclerosis, hypertension, a skin disease, an inflammation and autoimmune disease, and an inflammatory respiratory disease.

26. The use of claim 25, wherein the central nervous system disorder is selected from the group consisting of a neurodegenerative disease, a cerebrovascular disease, seizure, epilepsy, a viral disease, a neuroinflammatory disease, a brain tumour, a traumatic brain injury, and a rare metabolic disease.

27. The use according to claim 26, wherein the neurodegenerative disease is selected from the group consisting of leukodystrophy, amyotrophic lateral sclerosis (ALS), Parkinson’s disease, multiple sclerosis, Alzheimer's disease, Huntington's chorea, degenerative ataxia, multiple system atrophy, a motor neuron disease, neuromyelitis optica, NBIA (neurodegeneration and brain iron accumulation disorders), and neuromyopathy.

28. The use of claim 27, wherein the leukodystrophy is adrenoleukodystrophy (ALD or X-ALD); the degenerative ataxia is Friedreich's ataxia; and the motor neuron disease is selected from the group consisting of progressive bulbar palsy, pseudobulbar palsy, primary lateral sclerosis (PLS), progressive muscular atrophy, spinal muscular atrophy (SMA), post-polio syndrome (PPS)-Marie-Tooth disease, Guillan-Barré syndrome, and adrenomyeloneuropathy (AMN) .

29. The use of claim 26, wherein the central nervous system disorder is a cerebrovascular disease selected from the group consisting of global or local ischemia, intracerebral haemorrhage, stroke, and vascular dementia, a viral disease selected from the group consisting of meningitis, encephalitis, rabies, measles, mumps, poliomyelitis, herpes simplex, and varicella zoster, or a rare metabolic disease is selected from the group consisting of organic acidemias, fatty acid disorders and genetic mitochondrial disorders.

30. The use of claim 25, wherein the disease or disorder is nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH).

31. The use of claim 25, wherein said disease or disorder is a chronic granulomatous disorder, a polycystic ovary syndrome, a thyroid carcinoma, a thyroid autoimmune disorder, a pituitary adenoma, atherosclerosis, hypertension, a skin disease, an inflammation and autoimmune disease, or inflammatory respiratory disease

32. The use of claim 25, wherein the mitochondrial disease is a primary mitochondrial disorder selected from the group consisting of Rett syndrome, Alper's disease; Leber's hereditary optic neuropathy (LHON); Kearns-Sayre syndrome (KSS); Leigh's syndrome; Leigh-like syndrome; maternally inherited Leigh syndrome (MILS); mitochondrial depletion syndrome (MDS); mitochondrial DNA depletion syndrome (MDDS); mitochondrial encephalomyopathy; mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE); neuropathy, ataxia, and retinitis pigmentosa (NARP); Pearson syndrome; chronic progressive external opthalmoplegia (CPEO); dominant optic atrophy (DOA); autosomal dominant optic atrophy (ADOA); mitochondrial myopathy; cardiomyopathy; mitochondrial encephalopathy; myoclonic epilepsy; maternally inherited diabetes and deafness (MIDD); ataxia neuropathy spectrum; 3-methylglutaconic aciduria; sensoneural deafness; neuroradiological findings of Leigh-like syndrome (MEGDEL); SURF1 (COX definient Leigh syndrome due to complex IV surfeit protein deficiency); oxidative phosphorylation disorders; Berth syndrome; lethal infantile cardiomyopathy (LIC); pyruvate carboxylase deficiency; pyruvate dehydrogenase deficiency; POLG mutation; isolated or combined OXPHOS deficiencies with so far unsolved genetic defect including disturbed pyruvate oxidation and ATP plus PCr production rates; POLG2 mutation; carnitine-acyl-cartinine deficiency; carnitine deficiency; creatinine deficiency syndromes; Co-Enzyme Q10 deficiency; Complex I deficiency; Complex II deficiency; Complex III deficiency; Complex IV deficiency; Complex V deficiency; lactic acidosis; leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL); Luft disease; carnitine palmitoyltransferase (CPT I or CPT II) deficiency; short-chain acyl-CoA dehydrogenase deficiency (SCAD); short-chain 3-hydroxyacetyl-CoA dehydrogenase deficiency (SCHAD); medium-chain acyl-CoA dehydrogenase deficiency (MCAD); multiple acyl-CoA dehydrogenase deficiency (MADD); long-chain acyl-CoA

dehydrogenase deficiency (LCAD); very long-chain acyl-CoA dehydrogenase deficiency (VLCAD); trifunctional protein (TFP) deficiency; and glutaric aciduria Type II.

33. The use of claim 32, wherein the mitochondrial disease is selected from the group consisting of Rett syndrome; dominant optic atrophy (DOA); autosomal dominant optic atrophy (ADOA); Complex I deficiency; Leber hereditary optic neuropathy (LHON); Kearns-Sayre syndrome (KSS); Leigh's syndrome; mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE); neuropathy, ataxia, and retinitis pigmentosa (NARP); Pearson syndrome; and chronic progressive external opthalmoplegia (CPEO).

34. The use of claim 25, wherein the mitochondrial disease is a secondary mitochondrial disorder selected from the group consisting of Duchenne muscular dystrophy (DMD); Becker muscular dystrophy (BMD); myotonic dystrophy (BMD); congenital myopathies; glycogen storage disorders; spinal-bulbar muscular atrophy (SBMA); argininosuccinic aciduria; autism spectrum disorder (ASD); autoimmune diseases of the skin (such as pemphigus vulgaris and lupus); methylmalonic and propionic acidurias; disorders or purine and/or pyrimidine synthesis; facioscapulohumeral muscular dystrophy (FSHD); congenital muscular dystrophies; collagen VI muscular dystrophies (e.g., Ullrich congenital muscular dystrophy, Bethlem myopathy, oculopharyngeal distal, and Emery-Dreifuss); DiGeorge syndrome; and neuromuscular disorders (such as limb-girdle muscular dystrophy, inflammatory myopathies, Charcot Marie Tooth (CMT) neuropathy, and drug-induced peripheral neuropathies).

35. An oral dosage form, comprising an effective amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, wherein the effective amount provides the following upon administration once per day to a human patient in need thereof:

(a) the steady-state area under the curve (AUC_{ss}) of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient of 34 μg·h/mL to 300 μg·h/mL;

(b) the minimum steady-state plasma drug concentration ($C_{min\ ss}$) of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient of 55 to 9126 ng/mL; or

(c) the AUC_{ss} of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient of 34 µg·h/mL to 300 µg·h/mL, and the $C_{min\ ss}$ of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in plasma from the patient of 55 to 9126 ng/mL; and

the AUC_{ss} of (a), the $C_{min\ ss}$ of (b), or the AUC_{ss} and $C_{min\ ss}$ of (c) is measured after at least five days of orally administering 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, to the patient per day.

36. The oral dosage form of claim 35, comprising from 10 to 500 mg of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof.

37. The oral dosage form of claim 35 or 36, comprising from 50 to 500 mg of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof.

38. The oral dosage form of any one of claims 35-37, wherein the oral dosage form is solid.

39. The oral dosage form of claim 38, wherein the oral solid dosage form is a tablet, a capsule, a pill, or a plurality of granules.

40. The oral dosage form of any one of claims 35-37, wherein the oral dosage form is an oral solution or an oral suspension.

41. Use of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for

providing a therapeutically effective amount of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione to a patient in need thereof, wherein the plasma concentration of adiponectin in a sample obtained from the patient is determined to give a baseline concentration of the adiponectin; and

(a) said medicament comprising an amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient per day;

(b) a plasma sample is obtained from the patient after 5 days or more of administering according to (a);

(c) the plasma concentration of the adiponectin in the plasma sample obtained in (b) is determined; and

(d) a recalculated amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in milligrams, is to be administered based on the concentration of the adiponectin in the plasma sample obtained in (c), wherein:

(i) a greater amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in mg per day, is to be administered to the patient for an increase in the adiponectin of about 200% or less in (c) relative to the baseline concentration of the adiponectin;

(ii) a lesser amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in mg per day, is to be administered to the patient for an increase in the adiponectin of about 600% or more in (c) relative to the baseline concentration of the adiponectin; and

(iii) the same amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in mg per day, is to be administered to the patient for an increase in the adiponectin of 200% to 600% in (c) relative to the baseline concentration of the adiponectin.

42. Use of a therapeutically effective amount of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the manufacture of a medicament to be administered to a patient in need thereof, wherein:

(i) an amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient per day;

(ii) a plasma sample is obtained from the patient after at least 4 days of administering according to (i);

(iii) the plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the plasma sample obtained in (ii) is determined; and

(iv) a recalculated amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in milligrams, is to be administered to the patient per day as determined according to the Equation **1**:

$$\text{new amount in mg} = \text{SD} \times \left(\frac{\text{CMT}}{\text{PC}} \right) \qquad \text{Equation } \mathbf{1},$$

wherein:

SD is the amount of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, to be administered to the patient in (i) in mg;

CMT is the $C_{min\ target}$ in ng/mL of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione;

$C_{min\ target}$ = (target AUC in ng·h/mL x 0.0341 ± 20%) - 1104 ± 20%; and

PC is the plasma concentration in ng/mL of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione determined in (iii).

43. The use of claim 42, wherein the target AUC is 100 µg.h/mL to 300 µg.h/mL or 30 µg.h/mL to 100 µg.h/mL.

44. Use of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, in the manufacture of the medicament for providing a therapeutically effective amount of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione to a patient in need thereof, wherein an initial dose of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-

2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient once per day for 5 days or more; and

(a) a higher dose of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient once per day if the plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient is less than 149 µg.h/mL;

(b) a lower dose of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient once per day if the plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient is more than 241 µg.h/mL; or

(c) an unchanged dose of 5-[[4-[2-[5-acetylpyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione, or a pharmaceutically acceptable salt thereof, is to be administered to the patient once per day if the plasma concentration of 5-[[4-[2-[5-(1-hydroxyethyl)pyridin-2-yl]ethoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione in the patient is between 150 µg.h/mL and 240 µg.h/mL.