

7. Use of low dose pioglitazone in the manufacture of a pharmaceutical formulation for the treatment of cognitive impairment of the Alzheimer's type, wherein the low dose pioglitazone comprises from about 0.5 to about 9 milligrams of pioglitazone.
8. The use of claim 7, wherein said pharmaceutical formulation is a tablet.
9. The use of claim 7, wherein said pharmaceutical formulation is a capsule.
10. The use of claim 7, wherein said pharmaceutical formulation is a caplet.
11. The use of claim 7, wherein said pharmaceutical formulation is a liquid.
12. The use of claim 7, wherein said pharmaceutical formulation is a semi-solid.
13. The use of claim 7, wherein said pharmaceutical formulation is a solid.
14. The use of any one of claims 7-13, wherein said pioglitazone is to be administered at a dosage that provides an AUC of from about 0.15 $\mu\text{g}\cdot\text{h/mL}$ to about 3.6 $\mu\text{g}\cdot\text{h/mL}$.
15. Use of a composition comprising low dose pioglitazone in the manufacture of a medicament for the treatment of cognitive decline, wherein the composition comprises from about 0.5 to about 9 milligrams of pioglitazone.
16. Use of low dose pioglitazone in the manufacture of a medicament for treating cognitive impairment of the Alzheimer's type in a human subject in need thereof, wherein the composition low dose pioglitazone comprises from about 0.5 to about 9 milligrams of pioglitazone.
17. The use according to claim 16, wherein said treating comprises delaying the onset of cognitive impairment of the Alzheimer's type.

38. Use of low dose pioglitazone in the manufacture of a medicament for delaying the onset of mild cognitive impairment in a subject at risk of developing Alzheimer's disease comprising:

determining the presence of at least one genetic variant of the TOMM40 gene, wherein said genetic variant is an rs10524523 allele, wherein the presence of said at least one genetic variant indicates a risk of developing Alzheimer's disease; and wherein the low dose pioglitazone comprises from about 0.5 to about 9 milligrams of pioglitazone.

39. Use of low dose pioglitazone in the manufacture of a medicament for delaying the onset of amnestic mild cognitive impairment in a subject at risk of developing Alzheimer's disease comprising:

determining the presence of at least one genetic variant of the TOMM40 gene, wherein said genetic variant is an rs10524523 allele, wherein the presence of said at least one genetic variant indicates a risk of developing Alzheimer's disease; and wherein the low dose pioglitazone comprises from about 0.5 to about 9 milligrams of pioglitazone.

40. Use of low dose pioglitazone in the manufacture of a medicament ~~for~~delaying for delaying the onset of preclinical Alzheimer's disease in a subject at risk of developing Alzheimer's disease comprising:

determining the presence of at least one genetic variant of the TOMM40 gene, wherein said genetic variant is an rs10524523 allele, wherein the presence of said at least one genetic variant indicates a risk of developing Alzheimer's disease; and wherein the low dose pioglitazone comprises from about 0.5 to about 9 milligrams of pioglitazone.

67. The use according to any one of claims 37-42, wherein said subject has an increased risk of developing Alzheimer's disease as compared to a control subject.

68. The use according to claim 67, wherein said control subject carries at least one copy of the TOMM40 rs10524523 allele comprising a poly-T repeat that is less than 19 nucleotides in length.

69. The use according to claim 67, wherein said control subject does not have a copy of the TOMM40 rs10524523 allele comprising a poly-T repeat that is 19 or greater nucleotides in length.

70. The use according to claims 46-61, wherein the pharmaceutical formulation is a bioequivalent formulation.

71. The use according to claims 46-61, wherein the pharmaceutical formulation is a pharmaceutically equivalent formulation.

72. The use according to claims 46-61, wherein the pharmaceutical formulation is a therapeutically equivalent formulation.

73. The use according to claims 16 ~~and or~~ 31, ~~or and~~ the method of claim 34, wherein said low dose pioglitazone unit dosage comprises from 0.5 to 6 mg of pioglitazone.

74. The use according to claims 16 ~~and or~~ 31, ~~or and~~ the method of claim 34, wherein said low dose pioglitazone unit dosage comprises from 0.5 to 1.5 mg of pioglitazone.

75. The use of claim 16, wherein the subject has mild cognitive impairment.

76. The use of claim 16, wherein the subject has mild Alzheimer's disease.

77. The use of claim 3, wherein ~~determination of~~ said risk based upon the subject's age and rs10524523 genotype is determined by a method comprising ~~comprises~~

detecting from a biological sample of said subject the rs10524523 genotype of said subject, wherein each allele of the rs10524523 genotype is assigned as:

- (a) short (S, less than 19 T residues);
- (b) long (L, 19-29 residues); or
- (c) very long (VL, 30 or more residues); and

determining from said rs10524523 genotype whether said subject is at increased risk in developing cognitive impairment of the Alzheimer's type at said predetermined age or age range, wherein:

- (1) age greater than about 62 and L,L or L,VL indicates increased risk;
- (2) age greater than about 62 and VL,VL does not indicate increased risk;
- (3) age greater than about 74 and S,L indicates increased risk;
- (4) age greater than about 77 and S,S indicates increased risk; and
- (5) age greater than about 76 and S,VL indicates increased risk.

78. The use of claim 77, wherein said determining further comprises detecting from a biological sample of said subject the ApoE genotype of said subject, wherein the presence of an ApoE genotype of $\epsilon 2/\epsilon 2$ or $\epsilon 2/\epsilon 3$ indicates the subject is not at increased risk.

79. The use according to claims 1-31 or 37-78, wherein the pioglitazone comprises a pharmaceutically acceptable salt of pioglitazone.

80. The use according to claims 1-31 or 37-78 of claim 79, wherein the pioglitazone consists of a pharmaceutically acceptable salt of pioglitazone ~~comprises pioglitazone hydrochloride~~.

81. The method according to claims 34-36, wherein the pioglitazone comprises a

pharmaceutically acceptable salt of pioglitazone.

82. The method according to claims 34-36 ~~claim 81~~, wherein the pioglitazone consists of a pharmaceutically acceptable salt of pioglitazone ~~comprises pioglitazone-hydrochloride~~.

83. The use according to claim 79 or claim 80, wherein the pioglitazone comprises pioglitazone hydrochloride.
84. The method according to claim 81 or claim 82, wherein the pioglitazone comprises pioglitazone hydrochloride.
85. The use according to claims 1, 7, or 16, or the method according to claim 34, wherein the low dose pioglitazone comprises from 0.5 to 9 milligrams of pioglitazone.