Claims

1. A pharmaceutical composition for use for the treatment of a protein misfolding neurodegenerative disease (PMND) in a patient, which comprises a pharmaceutical carrier or vehicle and a fixed-dose combination of a dopamine-agonist Adverse Effects (or Events) Inhibitor (AEsI) selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof, in an amount equivalent to from 2 mg to 120 mg of domperidone base, and a dopamine agonist selected from the group consisting of pramipexole and pharmaceutically acceptable salts and solvates thereof, in an amount equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate.

2. The composition of claim 1, wherein said AEsI is selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof, in an amount equivalent to from 2 mg to 40 mg of domperidone base.

3. The composition according to any one of claims 1 and 2, wherein said AEsI is selected from the group consisting of domperidone base, domperidone maleate and domperidone succinate (1:1).

4. The composition according to any one of claims 1 to 3, wherein said dopamine agonist is pramipexole or a pharmaceutically acceptable salt thereof, in an amount equivalent to from 15 mg to 25 mg of pramipexole dihydrochloride monohydrate.

5. The composition of claim 4, wherein said pramipexole or pharmaceutically acceptable salt thereof is in an amount equivalent to from more than 20 mg to 25 mg of pramipexole dihydrochloride monohydrate.

6. The composition according to any one of claims 1 to 5, wherein said disease is a Parkinson's disease.

7. The composition according to any one of claims 1 to 5, wherein said disease is a Parkinson's disease related disorder selected from the group consisting of Restless Leg Syndrome, Dopamine-Responsive Dystonia Syndrome, Progressive Supranuclear Palsy, Fronto-temporal Lobe Dementia, and Corticobasal Degeneration.

8. The composition of claim 1, wherein said domperidone or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 2 mg to 40 mg of domperidone base; said pramipexole or pharmaceutically

acceptable salt or solvate thereof is present in an amount equivalent to from 0.125 mg to 6 mg of pramipexole dihydrochloride monohydrate; and said disease is Restless Leg Syndrome.

9. The composition of claim 8, wherein said pramipexole or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 0.125 mg to 1 mg of pramipexole dihydrochloride monohydrate.

10. Use of a dopamine-agonist Adverse Effects (or Events) Inhibitor (AEsI) selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of a protein misfolding neurodegenerative disease in a fixed-dose combination with pramipexole or a pharmaceutically acceptable salt thereof.

11. The use of claim 10, wherein, in said fixed-dose combination, domperidone or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 2 mg to 120 mg of domperidone base, and said pramipexole or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate.

12. The use of claim 10, wherein, in said fixed-dose combination, domperidone or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 2 mg to 120 mg of domperidone base, and said pramipexole or pharmaceutically acceptable salt or solvate thereof is present in an amount equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate.

13. A method for treating a disease selected from the group consisting of Parkinson's disease and Parkinson's disease-related disorders in a patient, which comprises administering to said patient at least one dopamine-agonist Adverse Effects (or Events) Inhibitor (AEsI) selected from the group consisting of peripheral DA-antagonists, 5HT3- antagonists, and NK-1 antagonists, in combination with a therapeutically effective daily dose of a dopamine agonist.

14. The method of claim 13, wherein said disease is Parkinson's disease, said AEsI is a peripheral DA-antagonist selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates and prodrugs thereof, at an effective daily dose equivalent to from 4 mg to 120 mg of domperidone

base and said dopamine agonist is selected from the group consisting of pramipexole and pharmaceutically acceptable salt and solvates thereof, at an effective daily dose of from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate.

15. The method of claim 14, wherein said AEsI is selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof, at an effective daily dose equivalent to from 4 mg to 120 mg of domperidone base; and said dopamine agonist is selected from the group consisting of pramipexole and pharmaceutically acceptable salt and solvates thereof, in an effective daily dose equivalent to from more than 4.5 mg to 45 mg of pramipexole dihydrochloride monohydrate.

16. The method of claim 14, wherein said AEsI and said dopamine agonist are each formulated in a pharmaceutical composition in dosage unit form, each in admixture with a pharmaceutical carrier or vehicle.

17. The method of claim 16, wherein said AEsI is selected from group consisting of domperidone and pharmaceutically acceptable salt and solvates thereof, in an amount per unit form equivalent to from 2 mg to 120 mg of domperidone base; and said dopamine agonist is pramipexole or a pharmaceutically acceptable salt thereof, in an amount per unit form equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate.

18. The method of claims 14, wherein said AEsI and said dopamine agonist are both formulated, as a fixed-dose combination, in a pharmaceutical composition comprising, as an active ingredient, domperidone Component (a), in an amount equivalent to from 2 mg to 120 mg of domperidone base; and, as a second active ingredient, ~~p~~ramipexole Component (b), in an amount equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate, in admixture with a pharmaceutical carrier or vehicle.

19. A fixed-dose combination consisting of a pharmaceutical composition comprising, as an active ingredient, domperidone Component (a), in an amount equivalent to from 2 mg to 120 mg of domperidone base; and, as a second active ingredient, ~~p~~ramipexole Component (b), in an amount equivalent to from 0.125 mg to 45 mg of pramipexole dihydrochloride monohydrate, in admixture with a pharmaceutical carrier or vehicle.

20. The use of a dopamine adverse effects inhibitor (AEsI) selected from

the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of a disease selected from the group consisting of Parkinson's disease and Parkinson's disease-related disorders, in combination with a dopamine agonist.

21. A dopamine adverse effects inhibitor (AEsI) selected from the group consisting of domperidone and pharmaceutically acceptable salts and solvates thereof for use for the treatment of a disease selected from the group consisting of Parkinson's disease and Parkinson's disease-related disorders, in combination with a dopamine agonist.

22. A kit comprising the fixed-dose combination of claim 19, and instructions for treatment of a Parkinson's disease or Parkinson's disease-related disorder.