preferred embodiments, the disclosure encompasses preventing, attenuating, and/or treating motor disorder side effects, including but not limited to dyskinesia, that are associated with L-DOPA therapy in Parkinson's patients (L-DOPA-induced dyskinesia, LID). The methods of the disclosure comprise administering to a patient in need thereof a therapeutic dose of a compound having agonist activity at both the 5-HT_{1a} and 5-HT_{1b} receptors (eltoprazine or batoprazine as non-limiting examples), or two separate compounds having agonist activity, one targeting the 5-HT_{1a} receptor, and another compound targeting the 5-HT_{1b} receptor.

[0009a] ~~In one aspect there is provided~~Disclosed is a use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating a movement or motor disorder or side effect thereof associated with administration of levodopa, or a dopamine-related drug, in a patient having Parkinson's disease, wherein said medicament is for administration of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof to said patient in need of treatment to reduce said movement or motor disorder or side effect thereof, wherein said dose of eltoprazine comprises from about 0.25 mg/day to about 25 mg/day.

[0009b] In one aspect, there is provided use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating a movement or motor disorder or side effect thereof associated with administration of levodopa, or a dopamine-related drug, in a patient having Parkinson's disease, wherein said medicament is for administration of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof of from 2.5 mg/day to 10 mg/day to said patient in need of treatment to reduce said movement or motor disorder or side effect thereof; wherein said medicament comprising eltoprazine is for administration prior to, concurrently with, or subsequent to the administration of at least one additional active ingredient to treat, attenuate, or prevent said movement or motor disorder or side effect thereof associated with administration of levodopa or said dopamine-related drug to said patient, wherein the administration of the medicament comprising eltoprazine in combination with the at least one additional active ingredient results in a reduction of the dose of levodopa, or a dopamine-related drug needed to treat a movement or motor disorder or side effect thereof in the patient; and wherein said at least one additional active ingredient is selected from the group consisting of:

- an (mTOR) complex 1 (mTORC1) inhibitor;
- a 5-HT1a/2a/alpha-2 antagonist;
- a 5-HT2a inverse agonist;
- an adenosine A2a receptor antagonist;
- an alpha-1 adrenoceptor antagonist;
- an alpha-2 adrenergic receptor antagonist;
- an AMPA antagonist;
- an AMPA/kainite antagonist;
- an anticonvulsant;
- a beta-2 antagonist;
- a CB agonist;
- a D2/5-HT2A+ antagonist;
- a dopaminergic stabilizer;
- a dopaminergic function enhancer/glutamate release inhibitor;

a combinations of a MAO-B inhibitor and an acetylcholinesterase inhibitor;
an acetylcholinesterase inhibitor;
a cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase;
an H2 antagonist;
a kynurenic hydroxylase inhibitor;
an L-type Ca2+ antagonist or L-type calcium channel blocker;
an mGluR5 antagonist;
a monoamine reuptake inhibitor;
a mu opioid receptor agonist
a nicotinic acetylcholine receptor (nAChR) modulator;
a nicotinic antagonist;
a nitric oxide synthase inhibitor;
a nootropic compound;
an NR1A/2B NMDA antagonist;
an NR2B selective NMDA antagonist;
an omega-3 fatty acid;
an opiate antagonist;
an anticholinergic;
an SSRI (Selective Serotonin Reuptake Inhibitor);
a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor;
a phosphodiesterase (PDE) inhibitor such as a phosphodiesterase 4 (PDE4) inhibitor or a phosphodiesterase 2 (PDE2) inhibitor; and
carbidopa.

[~~0009b~~0009c] ~~In one aspect, there is provided~~Disclosed is a use of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating Parkinson's disease in a human subject in need thereof, wherein said medicament is to be administered with a dose of levodopa to said human subject, wherein said dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof comprises from 0.25 mg/day to 25 mg/day.

[~~0009c~~0009d] In one aspect, there is provided use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating, attenuating, or preventing a movement or motor disorder, or side effect thereof associated with administration of levodopa (L-DOPA), a dopamine-related drug, or a non-L-DOPA-related drug to a patient having Parkinson's disease, wherein said medicament is for use in combination with deep brain stimulation and/or transcranial magnetic stimulation and wherein said eltoprazine or a pharmaceutically acceptable acid addition salt thereof is administered to the patient in a dose of from 2.5 mg/day to 10 mg/day.

The methods of the

disclosure also encompass preventing, attenuating, and/or treating PD in a patient in need thereof.

[0010] The disclosure encompasses many possible administration and dosage regimes, with administration strategies including, but not limited to, administration of the 5-$HT_{1a/1b}$ receptor agonist or partial agonist before or after initiation of L-DOPA or other dopamine-related drug administration, and administration of the 5-$HT_{1a/1b}$ receptor agonist or partial agonist before or after development of motor disorder side effects. Dosage strategies include therapeutic and sub-therapeutic dosages of L-DOPA or other dopamine-related drug. In certain embodiments, this disclosure encompasses a reduction in the dosage of L-DOPA or other dopamine-related drug after administration of the 5-$HT_{1a/1b}$ receptor agonist or partial agonist. In instances where eltoprazine is used as the 5-$HT_{1a/1b}$ receptor agonist, non-limiting examples of daily dosages include, 2.5 mg, 5.0 mg, 7.5 mg, and 10 mg as embodiments within the scope of the disclosure. Particularly preferred dosages of eltoprazine, in humans, are 5 mg/day and 7.5 mg/day. Administration schedules may also be altered to achieve a therapeutically effective concentration of compound to treat the disorder or symptoms described herein. In some embodiments, for example, the compound may be administered once per day, twice per day, thrice per day, 4 times per day, 5 times per day, 7 times per day or 10 times per day.

[0011] Kits comprising one or more of the following are also encompassed by the disclosure described herein: a compound having agonist activity at both the 5-HT_{1a} and 5-HT_{1b} receptors, or two separate compounds having agonist activity, one targeting the 5-HT_{1a} receptor, and another compound targeting the 5-HT_{1b} receptor, additional compounds, L-DOPA or other or other dopamine-related drug, and instructions for administration.

[0011a] ~~In one aspect, there is provided~~Disclosed is a kit comprising therapeutically effective dosages of eltoprazine and levodopa, and further comprising instructions for use in administering said eltoprazine and said levodopa to a subject with Parkinson's disease.

Non-limiting examples of

such kits include a kit comprising eltoprazine, and a kit comprising eltoprazine, L-DOPA, a

Claims:

1. Use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating a movement or motor disorder or side effect thereof associated with administration of levodopa, or a dopamine-related drug, in a patient having Parkinson's disease, wherein said medicament is for administration of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof to said patient in need of treatment to reduce said movement or motor disorder or side effect thereof, wherein said dose of eltoprazine comprises from about 0.25 mg/day to about 25 mg/day.

2. The use according to claim 1, wherein said movement or motor disorder or side effect thereof is dyskinesia or hyperkinesia.

3. The use according to claim 1, wherein said dose of eltoprazine comprises from about 2.5 mg/day to about 10 mg/day.

4. The use according to claim 3, wherein said dose of eltoprazine comprises about 2.5 mg/day.

5. The use according to claim 3, wherein said dose of eltoprazine comprises about 5.0 mg/day. of eltoprazine

6. The use according to claim 3, wherein said dose of eltoprazine comprises about 7.5 mg/day.

7. The use according to claim 3, wherein said dose of eltoprazine comprises about 10 mg/day.

8. The use according to any one of claims 1 to 7, wherein said patient is human.

9. The use according to claim 1 or claim 8, wherein said eltoprazine administration does not reduce efficacy of said levodopa or dopamine-related drug administration.

10. Use of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof

in the manufacture of a medicament for treating Parkinson's disease in a human subject in need thereof, wherein said medicament is to be administered with a dose of levodopa to said human subject, wherein said dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof comprises from 0.25 mg/day to 25 mg/day.

11. The use according to claim 10, wherein said eltoprazine and said levodopa are concurrently active in said human subject.

12. The use according to claim 10 or claim 11, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration to said human subject before said human subject develops dyskinesia associated with said levodopa administration.

13. The use according to claim 10 or claim 11, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration to said human subject after said human subject develops dyskinesia associated with said levodopa administration.

14. The use according to claim 10 or claim 11, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine to said human subject before the administration of said medicament comprising levodopa.

15. The use according to any one of claims 10 to 14, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine at a dose from about 2.5 mg/day to about 10 mg/day.

16. The use according to claim 15, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine at a dose of about 2.5 mg/day.

17. The use according to claim 15, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine at a dose of about 5.0 mg/day.

18. The use according to claim 15, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine

at a dose of about 7.5 mg/day.

19. The use according to claim 15, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration of eltoprazine at a dose of about 10 mg/day.

20. The use according to any one of claims 1 to 19, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration prior to, concurrently with, or subsequent to the administration of at least one additional active ingredient for use in treating, attenuating, or preventing said movement or motor disorder or side effect thereof associated with administration of levodopa or said dopamine-related drug to said patient, wherein said at least one additional active ingredient is selected from the group consisting of:

an (mTOR) complex 1 (mTORC1) inhibitor;
a 5-HT1a/2a/alpha-2 antagonist;
a 5-HT2a inverse agonist;
an adenosine A2a receptor antagonist;
an alpha-1 adrenoceptor antagonist;
an alpha-2 adrenergic receptor antagonist;
an AMPA antagonist;
an AMPA/kainite antagonist;
an anticonvulsant;
a beta-2 antagonist;
a CB agonist;
a D2/5-HT2A+ antagonist;
a dopaminergic stabilizer;
a dopaminergic function enhancer/glutamate release inhibitor;
a combinations of a MAO-B inhibitor and an acetylcholinesterase inhibitor;
an acetylcholinesterase inhibitor;
a cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase;
an H2 antagonist;

a kynurenic hydroxylase inhibitor;

an L-type Ca2+ antagonist or L-type calcium channel blocker;

an mGluR5 antagonist;

a monoamine reuptake inhibitor;

a mu opioid receptor agonist

a nicotinic acetylcholine receptor (nAChR) modulator;

a nitric oxide synthase inhibitor;

a nootropic compound;

an NR1A/2B NMDA antagonist;

an NR2B selective NMDA antagonist;

an omega-3 fatty acid;

an opiate antagonist;

an anticholinergic;

an SSRI (Selective Serotonin Reuptake Inhibitor);

a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor;

a phosphodiesterase (PDE) inhibitor such as a phosphodiesterase 4 (PDE4) inhibitor or a phosphodiesterase 2 (PDE2) inhibitor; and

carbidopa.

21. The use according to claim 20,

wherein the (mTOR) complex 1 (mTORC1) inhibitor is rapamycin;

wherein the 5-HT1a/2a/alpha-2 antagonist is mirtazapine;

wherein the 5-HT2a inverse agonist is selected from ACP103 (pimvaserin), nelotanserin, eplivanserin, or AC-90179 [2-(4-Methoxyphenyl)-N-(4-methyl-benzyl)-N- (1-methyl-piperidin-4-yl)-acetamide Hydrochloride]);

wherein the adenosine A2a receptor antagonist is selected from istradefylline (KW-6002), SYN-115 (4-Hydroxy-N-[4-methoxy-7-(4-morpholinyl)-2-benzothiazolyl]-4-methyl-1-piperidinecarboxamide, (Synosia Therapeutics), preladenant (SCH420814), ZM-241,385 (4-(2-[7-amino-2-(2-furyl) [1,2,4]-triazolo[2,3- a][1,3,5]triazin- 5-yl amino]ethyl) phenol), VER-7835 (2-amino-6-(furan-2-yl)-N- (thiophen-2-ylmethyl)-9H-purine-9- carboxamide), MSX-3 (3-(3-

hydroxypropyl)-7- methyl-8-(m-methoxystyryl)-1-propargylxanthine), or ST-1535 (2-butyl-9-methyl-8-(2H- 1,2,3-triazol 2-yl)-9 H-purin-6-ylamine));

wherein the alpha-1 adrenoceptor antagonist is selected from HEAT (2-[[beta-(-4-hydroxyphenyl)ethyl]aminomethyl]-1-tetralone), alfuzosin, doxazosin, moxisylyte, prazosin, or trimazosin;

wherein the alpha-2 adrenergic receptor antagonist is selected from idazoxan, fipamezole (JP1730), atipamezole, mianserin, phentolamine, or tolazoline;

wherein the AMPA antagonist is E2007 (perampanel);

wherein the AMPA/kainite antagonist is LY300164 [7-acetyl-5-(4-aminophenyl)-8,9-dihydro-8-methyl-7H-1,3-dioxolo(4,5H)-2,3-benzodiazepine];

wherein the anticonvulsant is selected from primidone, zonisamide, levetiracetam, mesuximide, eslicarbazepine acetate, or pregabalin;

wherein the beta-2 antagonist is selected from propranolol, alprenolol, carteolol, nadolol, sotalol, or timolol;

wherein the CB agonist is selected from nabilone or WIN55,212-2 ((R)-(+)-[2,3-Dihydro-5-methyl-3-(4-morpholinylmethyl)pyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]-1-naphthalenylmethanone mesylate);

wherein the D2/5-HT2A+ antagonist is clozapine or quetiapine;

wherein the dopaminergic stabilizer is selected from ACR325, aripiprazole, or pridopidine;

wherein the dopaminergic function enhancer/glutamate release inhibitor is safinamide;

wherein the combination of the MAO-B inhibitor and acetylcholinesterase inhibitor is selected from rasagiline, selegiline, safinamide, or EVT-302 (Evotec AG) in combination with ladostigil (TV-3326);

wherein the acetylcholinesterase inhibitor is doepezil;

wherein the cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase is rivastigmine;

wherein the H2 antagonist is selected from famotidine, cimetidine, burimamide, ranitidine, or metiamide;

wherein the kynurenic hydroxylase inhibitor is selected from Ro 61-8048 (3,4-Dimethoxy-N-[4-(3-nitrophenyl)-2-thiazolyl]benzene sulfonamide or FCE 28833 [(R,S)-2-amino-4-oxo-4-(3',4'-dichlorophenyl) butanoic acid];

wherein the L-type Ca2+ antagonist or L-type calcium channel blocker is selected from isradipine, amlodipine, azelnidipine, cilnidipine, lacidipine, nimodipine, nilvadipine or topiramate;

wherein the mGluR5 antagonist is AFQ056 (6-methyl-2-(phenylethynyl)pyridine);

wherein the monoamine reuptake inhibitor is selected from NS2330 (tesofensine), bicifadine, or DOV-102,677 [(5R)-5-(3,4-dichlorophenyl)bicyclo[3.1.0]hexane];

wherein the nicotinic acetylcholine receptor (nAChR) modulator is selected from an nAChR selective or non-selective agonist; an nAChR selective or non-selective partial agonist; an nAChR competitive antagonist; an nAChR non-competitive antagonist; nicotine (NP002); acetylcholine; choline; epibatidine; lobeline; varenicline; sazetidine-A; DMXB-A (GTS-21, 3-2,4 dimethoxybenzylidene); or SIB-1508Y (3-Ethynyl-5-[(2S)-1-methyl-2-pyrrolidinyl]pyridine);

wherein the nicotinic antagonist is selected from chlorisondamine, d-tubocurarine, mecamylamine, or bupropion;

wherein the nitric oxide synthase inhibitor is selected from 7-nitroindazole or NG-nitro-L-arginine;

wherein the nootropic compound is levitircetam;

wherein the NR1A/2B NMDA antagonist is Cl-1041 (5-[2-[4-(4-fluorobenzyl)piperidin-1-yl]ethylsulfinyl]-2,3-dihydro-1H-benzimidazol-2-one));

wherein the NR2B selective NMDA antagonist is selected from MK0657, CP-101,606 (traxoprodil), eliprodil, Ro 25-6981 ((±)-(R*,S*)-α-(4-hydroxyphenyl)-β-methyl-4-(phenylmethyl)-1-piperidine propanol), EVT-101 (Evotec AG), or EVT-103 (Evotec

wherein the omega-3 fatty acid is docosahexaenoic acid;

wherein the opiate antagonist is naltrexone;

wherein the anticholinergic is selected from amantadine, ipratropium bromide, oxitropium bromide, or tiotropium;

wherein the SSRI is selected from fluoxetine, paroxetine, sertraline, escitalopram, citalopram, or fluvoxamine;

wherein the 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor is SYN-118, (Synosia Therapeutics);

wherein the PDE4 inhibitor is selected from ronomilast, roflumilast, mesembrine, rolipram, ibudilast, piclamilast, luteolin, cilomilast, tofimilast (9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9H-pyrazolo(3,4-c)-1,2,4-triazolo(4,3-a)pyridine), tipelukast, ibudilast, apremilast ((S)-N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-methanesulfonylethyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl] acetamide, Celgene Corporation), CC-1088 (a thalidomide analog inhibitor of PDE4, Celgene Corporation), 8-biarylnaphthyridinones such as MK-0952 (Merck), DC-AT-46 (7-benzylamino-6-chloro-2 piperazino-4-pyrrolidino-pteridine), HT-0712 ((3R,5R)-5-(3-(cyclopentyloxy)-4-methoxyphenyl)-3-(3-methylbenzyl)piperidin-2-one, Helicon Therapeutics, Inc.), MEM-1414 (Roche), MEM-1917 (Roche), MEM-1018 (Roche), MEM-1091 (Roche), or DG071 (decode Genetics); and

wherein the PDE2 inhibitor is BAY 60-7550.

22. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one anticonvulsant, which is, optionally, selected from primidone or zonisamide.

23. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one mGluR5 antagonist, which is, optionally, AFQ056.

24. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one L-type calcium channel blocker, which is, optionally, selected from isradipine, nimodapine, or nilvadipine.

25. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one NR2B selective NMDA antagonist, which is, optionally, selected from Ro 25-6981, EVT-101, or EVT-103.

26. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of (i) at least one adenosine A2a receptor antagonist, which is, optionally, selected from istradefylline (KW-6002), SYN-115 (4-Hydroxy-N-[4-methoxy-7-(4-morpholinyl)-2-benzothiazolyl]-4-methyl-1-piperidinecarboxamide, or preladenant (SCH420814); or (ii) at least one alpha-2 adrenergic receptor antagonist, which is, optionally, selected from fipamezole (JP1730) or idazoxan.

27. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor, which is, optionally, SYN-118.

28. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one nicotinic acetylcholine receptor (nAChR) modulator, which is, optionally, selected from an nAChR selective or non-selective agonist; an nAChR selective or non-selective partial agonist; an nAChR competitive antagonist; an nAChR non-competitive antagonist; nicotine (NP002); acetylcholine; choline; epibatidine; lobeline; varenicline; or sazetidine-A.

29. The use according to claim 20 or claim 21, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one phosphodiesterase (PDE) inhibitor, which is, optionally, a phosphodiesterase 2 (PDE2) inhibitor or a phosphodiesterase 4 (PDE4) inhibitor.

30. The use according to any one of claims 20 to 29, wherein said administration of said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one additional active ingredient is an administration mode selected from:

(i) administration of said medicament to said patient in need thereof before said patient develops a movement or motor disorder, or side effect thereof, associated with levodopa administration; or

(ii) administration of said medicament to said patient in need thereof after said patient develops a movement or motor disorder, or side effect thereof, associated with levodopa administration.

31. The use according to any one of claims 20 to 30, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is for administration to the patient in a dosing regimen selected from:

(i) administration of said eltoprazine or a pharmaceutically acceptable acid addition salt thereof to the patient before said at least one additional active agent is administered;

(ii) administration of said eltoprazine or a pharmaceutically acceptable acid addition salt thereof to the patient after said at least one additional active agent is administered;

(iii) administration of said eltoprazine or a pharmaceutically acceptable acid addition salt thereof to the patient concurrently with the administration of said at least one additional active agent.

32. Use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating, attenuating, or preventing a movement or motor disorder, or side effect thereof associated with administration of levodopa (L-DOPA), a dopamine-related drug, or a non-L-DOPA-related drug to a patient having Parkinson's disease, wherein said medicament is for use in combination with deep brain stimulation and/or transcranial magnetic stimulation.

33. The use according to claim 32, wherein the order of treatment comprises an administration regimen selected from:

(i) said deep brain stimulation and/or transcranial magnetic stimulation precedes treatment of the patient with levodopa (L-DOPA), an L-DOPA-related drug, or a non-L-DOPA-related drug;

(ii) said deep brain stimulation and/or transcranial magnetic stimulation follows treatment of the patient with levodopa (L-DOPA), an L-DOPA-related drug, or a non-L-DOPA-related drug;

(iii) said deep brain stimulation and/or transcranial magnetic stimulation precedes treatment of the patient with eltoprazine or a pharmaceutically acceptable acid addition salt thereof; or

(iv) said deep brain stimulation and/or transcranial magnetic stimulation follows treatment of the patient with eltoprazine or a pharmaceutically acceptable acid addition salt thereof.

34. The use according to any one of claims 1 to 33, wherein said dopamine-related drug is selected from a dopamine receptor agonist, which is, optionally, bromocriptine, pergolide, cabergoline, apomorphine, or lisuride; or a non-ergoline dopamine agonist, which is, optionally, ropinirole or pramipexole.

35. A kit comprising therapeutically effective dosages of eltoprazine and levodopa, and further comprising instructions for use in administering said eltoprazine and said levodopa to a subject with Parkinson's disease.

Claims

1. Use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating a movement or motor disorder or side effect thereof associated with administration of levodopa, or a dopamine-related drug, in a patient having Parkinson's disease, wherein said medicament is for administration of a dose of eltoprazine or a pharmaceutically acceptable acid addition salt thereof of from 2.5 mg/day to 10 mg/day to said patient in need of treatment to reduce said movement or motor disorder or side effect thereof; wherein said medicament comprising eltoprazine is for administration prior to, concurrently with, or subsequent to the administration of at least one additional active ingredient to treat, attenuate, or prevent said movement or motor disorder or side effect thereof associated with administration of levodopa or said dopamine-related drug to said patient, wherein the administration of the medicament comprising eltoprazine in combination with the at least one additional active ingredient results in a reduction of the dose of levodopa, or a dopamine-related drug needed to treat a movement or motor disorder or side effect thereof in the patient; and wherein said at least one additional active ingredient is selected from the group consisting of:

an (mTOR) complex 1 (mTORC1) inhibitor;

a 5-HT1a/2a/alpha-2 antagonist;

a 5-HT2a inverse agonist;

an adenosine A2a receptor antagonist;

an alpha-1 adrenoceptor antagonist;

an alpha-2 adrenergic receptor antagonist;

an AMPA antagonist;

an AMPA/kainite antagonist;

an anticonvulsant;

a beta-2 antagonist;

a CB agonist;

a D2/5-HT2A+ antagonist;

a dopaminergic stabilizer;

a dopaminergic function enhancer/glutamate release inhibitor;

a combinations of a MAO-B inhibitor and an acetylcholinesterase inhibitor;

an acetylcholinesterase inhibitor;

a cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase;

an H2 antagonist;

a kynurenic hydroxylase inhibitor;

an L-type Ca2+ antagonist or L-type calcium channel blocker;

an mGluR5 antagonist;

a monoamine reuptake inhibitor;

a mu opioid receptor agonist

a nicotinic acetylcholine receptor (nAChR) modulator;

a nicotinic antagonist;

a nitric oxide synthase inhibitor;

a nootropic compound;

an NR1A/2B NMDA antagonist;

an NR2B selective NMDA antagonist;

an omega-3 fatty acid;

an opiate antagonist;

an anticholinergic;

an SSRI (Selective Serotonin Reuptake Inhibitor);

a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor;

a phosphodiesterase (PDE) inhibitor such as a phosphodiesterase 4 (PDE4) inhibitor or a phosphodiesterase 2 (PDE2) inhibitor; and

carbidopa.

2. The use according to claim 1,

wherein the (mTOR) complex 1 (mTORC1) inhibitor is rapamycin;

wherein the 5-HT1a/2a/alpha-2 antagonist is mirtazapine;

wherein the 5-HT2a inverse agonist is selected from ACP103 (pimvaserin), nelotanserin, eplivanserin, or AC-90179 [2-(4-Methoxyphenyl)-N-(4-methyl-benzyl)-N-(1-methyl-piperidin-4-yl)-acetamide Hydrochloride]);

wherein the adenosine A2a receptor antagonist is selected from istradefylline (KW-2,3-triazol 2-yl)-9 H-purin-6-ylamine));

wherein the alpha-1 adrenoceptor antagonist is selected from HEAT (2-[[beta-(-4-hydroxyphenyl)ethyl]aminomethyl]-1-tetralone), alfuzosin, doxazosin, moxisylyte, prazosin, or trimazosin;

wherein the alpha-2 adrenergic receptor antagonist is selected from idazoxan, fipamezole (JP1730), atipamezole, mianserin, phentolamine, or tolazoline;

wherein the AMPA antagonist is E2007 (perampanel);

wherein the AMPA/kainite antagonist is LY300164 [7-acetyl-5-(4-aminophenyl)-8,9-dihydro-8-methyl-7H-1,3-dioxolo(4,5H)-2,3-benzodiazepine];

wherein the anticonvulsant is selected from primidone, zonisamide, levetiracetam, mesuximide, eslicarbazepine acetate, or pregabalin;

wherein the beta-2 antagonist is selected from propranolol, alprenolol, carteolol, nadolol, sotalol, or timolol;

wherein the CB agonist is selected from nabilone or WIN55,212-2 ((R)-(+)-[2,3-Dihydro-5-methyl-3-(4-morpholinylmethyl)pyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]-1-naphthalenylmethanone mesylate);

wherein the D2/5-HT2A+ antagonist is clozapine or quetiapine;

wherein the dopaminergic stabilizer is selected from ACR325, aripiprazole, or pridopidine;

wherein the dopaminergic function enhancer/glutamate release inhibitor is safinamide;

wherein the combination of the MAO-B inhibitor and acetylcholinesterase inhibitor is selected from rasagiline, selegiline, safinamide, or EVT-302 (Evotec AG) in combination with ladostigil (TV-3326);

wherein the acetylcholinesterase inhibitor is doepezil;

wherein the cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase is rivastigmine;

wherein the H2 antagonist is selected from famotidine, cimetidine, burimamide, ranitidine, or metiamide;

wherein the kynurenic hydroxylase inhibitor is selected from Ro 61-8048 (3,4-Dimethoxy-N-[4-(3-nitrophenyl)-2-thiazolyl]benzene sulfonamide or FCE 28833 [(R,S)-2-amino-4-oxo-4-(3',4'-dichlorophenyl) butanoic acid];

wherein the L-type Ca2+ antagonist or L-type calcium channel blocker is selected from isradipine, amlodipine, azelnidipine, cilnidipine, lacidipine, nimodipine, nilvadipine or topiramate;

wherein the mGluR5 antagonist is AFQ056 (6-methyl-2-(phenylethynyl)pyridine);

wherein the monoamine reuptake inhibitor is selected from NS2330 (tesofensine), bicifadine, or DOV-102,677 [(5R)-5-(3,4-dichlorophenyl)bicyclo[3.1.0]hexane];

wherein the nicotinic acetylcholine receptor (nAChR) modulator is selected from an nAChR selective or non-selective agonist; an nAChR selective or non-selective partial agonist; an nAChR competitive antagonist; an nAChR non-competitive antagonist; nicotine (NP002); acetylcholine; choline; epibatidine; lobeline; varenicline; sazetidine-A; DMXB-A (GTS-21, 3-2,4 dimethoxybenzylidene); or SIB-1508Y (3-Ethynyl-5-[(2S)-1-methyl-2-pyrrolidinyl]pyridine);

wherein the nicotinic antagonist is selected from chlorisondamine, d-tubocurarine, mecamylamine, or bupropion;

wherein the nitric oxide synthase inhibitor is selected from 7-nitroindazole or NG-nitro-L-arginine;

wherein the nootropic compound is levitircetam;

wherein the NR1A/2B NMDA antagonist is Cl-1041 (5-[2-[4-(4-fluorobenzyl)piperidin-1-yl]ethylsulfinyl]-2,3-dihydro-1H-benzimidazol-2-one));

wherein the NR2B selective NMDA antagonist is selected from MK0657, CP-101,606 (traxoprodil), eliprodil, Ro 25-6981 ((±)-(R*,S*)-α-(4-hydroxyphenyl)-β-methyl-4-(phenylmethyl)-1-piperidine propanol), EVT-101 (Evotec AG), or EVT-103 (Evotec wherein the omega-3 fatty acid is docosahexaenoic acid;

wherein the opiate antagonist is naltrexone;

wherein the anticholinergic is selected from amantadine, ipratropium bromide, oxitropium bromide, or tiotropium;

wherein the SSRI is selected from fluoxetine, paroxetine, sertraline, escitalopram, citalopram, or fluvoxamine;

wherein the 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor is SYN-118, (Synosia Therapeutics);

wherein the PDE4 inhibitor is selected from ronomilast, roflumilast, mesembrine, rolipram, ibudilast, piclamilast, luteolin, cilomilast, tofimilast (9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9H-pyrazolo(3,4-c)-1,2,4-triazolo(4,3-a)pyridine), tipelukast, ibudilast, apremilast ((S)-N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-methanesulfonylethyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl] acetamide, Celgene Corporation), CC-1088 (a thalidomide analog inhibitor of PDE4, Celgene Corporation), 8-biarylnaphthyridinones such as MK-0952 (Merck), DC-AT-46 (7-benzylamino-6-chloro-2 piperazino-4-pyrrolidino-pteridine), HT-0712 ((3R,5R)-5-(3-(cyclopentyloxy)-4-methoxyphenyl)-3-(3-methylbenzyl)piperidin-2-one, Helicon Therapeutics, Inc.), MEM-1414 (Roche), MEM-1917 (Roche), MEM-1018 (Roche), MEM-1091 (Roche), or DG071 (decode Genetics); and

wherein the PDE2 inhibitor is BAY 60-7550.

3. The use according to claim 1 or claim 2, wherein said movement or motor disorder or side effect thereof is dyskinesia or hyperkinesia.

4. The use according to any one of claims 1 to 3, wherein said dose of eltoprazine is from 2.5 mg/day to 7.5 mg/day.

5. The use according to claim 4, wherein said dose of eltoprazine is 2.5 mg/day.

6. The use according to claim 4, wherein said dose of eltoprazine is 5.0 mg/day.

7. The use according to claim 4, wherein said dose of eltoprazine is 7.5 mg/day.

8. The use according to claim 4, wherein said dose of eltoprazine is 10 mg/day.

9. The use according to any one of claims 1 to 8, wherein said patient is human.

10. The use according to claim 9, wherein said eltoprazine administration does not reduce efficacy of said levodopa or dopamine-related drug administration.

11. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to,

concurrently with, or subsequent to administration of at least one anticonvulsant, which is, optionally, selected from primidone or zonisamide.

12. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one mGluR5 antagonist, which is, optionally, AFQ056.

13. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one L-type calcium channel blocker, which is, optionally, selected from isradipine, nimodapine, or nilvadipine.

14. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one NR2B selective NMDA antagonist, which is, optionally, selected from Ro 25-6981, EVT-101, or EVT-103.

15. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of (i) at least one adenosine A2a receptor antagonist, which is, optionally, selected from istradefylline (KW-6002), SYN-115 (4-Hydroxy-N-[4-methoxy-7-(4-morpholinyl)-2-benzothiazolyl]-4-methyl-1-piperidinecarboxamide, or preladenant (SCH420814); or (ii) at least one alpha-2 adrenergic receptor antagonist, which is, optionally, selected from fipamezole (JP1730) or idazoxan.

16. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor, which is, optionally, SYN-118.

17. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to,

concurrently with, or subsequent to administration of at least one nicotinic acetylcholine receptor (nAChR) modulator, which is, optionally, selected from an nAChR selective or non-selective agonist; an nAChR selective or non-selective partial agonist; an nAChR competitive antagonist; an nAChR non-competitive antagonist; nicotine (NP002); acetylcholine; choline; epibatidine; lobeline; varenicline; or sazetidine-A.

18. The use according to claim 9, wherein said medicament is for administration of eltoprazine or a pharmaceutically acceptable acid addition salt thereof prior to, concurrently with, or subsequent to administration of at least one phosphodiesterase (PDE) inhibitor, which is, optionally, a phosphodiesterase 2 (PDE2) inhibitor or a phosphodiesterase 4 (PDE4) inhibitor.

19. The use according to any one of claims 1 to 18, wherein said medicament comprising eltoprazine or a pharmaceutically acceptable acid addition salt thereof is administered to said patient prior to, concurrently with, or subsequent to the administration of said at least one additional active ingredient; and wherein the administration of said medicament is before or after said patient develops a movement or motor disorder, or side effect thereof, associated with levodopa administration.

20. Use of eltoprazine or a pharmaceutically acceptable acid addition salt thereof in the manufacture of a medicament for treating, attenuating, or preventing a movement or motor disorder, or side effect thereof associated with administration of levodopa (L-DOPA), a dopamine-related drug, or a non-L-DOPA-related drug to a patient having Parkinson's disease, wherein said medicament is for use in combination with deep brain stimulation and/or transcranial magnetic stimulation and wherein said eltoprazine or a pharmaceutically acceptable acid addition salt thereof is administered to the patient in a dose of from 2.5 mg/day to 10 mg/day.

21. The use according to claim 20, wherein the order of treatment comprises an administration regimen selected from:

(i) said deep brain stimulation and/or transcranial magnetic stimulation precedes treatment of the patient with levodopa (L-DOPA), an L-DOPA-related drug, or a non-L-DOPA-related drug;

(ii) said deep brain stimulation and/or transcranial magnetic stimulation follows treatment of the patient with levodopa (L-DOPA), an L-DOPA-related drug, or a non-L-DOPA-related drug;

(iii) said deep brain stimulation and/or transcranial magnetic stimulation precedes treatment of the patient with eltoprazine or a pharmaceutically acceptable acid addition salt thereof; or

(iv) said deep brain stimulation and/or transcranial magnetic stimulation follows treatment of the patient with eltoprazine or a pharmaceutically acceptable acid addition salt thereof.

22. The use according to claim 20 or claim 21, wherein said medicament comprises eltoprazine or a pharmaceutically acceptable acid addition salt thereof at a dose of from 5 mg/day to 7.5 mg/day.

23. The use according to any one of claims 1 to 22, wherein said dopamine-related drug is selected from a dopamine receptor agonist, which is, optionally, bromocriptine, pergolide, cabergoline, apomorphine, or lisuride; or a non-ergoline dopamine agonist, which is, optionally, ropinirole or pramipexole.