salt and/or isotopic variant thereof, to a patient in need thereof wherein the patient is also being administered digoxin, comprising: administering to the patient a therapeutically effective amount of the VMAT2 inhibitor.

[0006] Also provided is a method of administering a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+)-α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, to a patient in need thereof, comprising: administering to the patient a therapeutically effective amount of the VMAT2 inhibitor, subsequently determining that the patient is to begin treatment with digoxin, and continuing administration of the therapeutically effective amount of the VMAT2 inhibitor to the patient.

[0007] Also provided is a method of administering a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+)-α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, to a patient in need thereof wherein the patient is also being administered digoxin, comprising: administering a therapeutically effective amount of the VMAT2 inhibitor to the patient, wherein the administration produces a mean digoxin C_{max} that is about 1.5 to 2.5 fold higher than the mean digoxin C_{max} for a patient who is administered digoxin alone and/or a mean digoxin $AUC_{0-\infty}$ that is about 1 to about 2 fold higher than the mean digoxin $AUC_{0-\infty}$ for a patient who is administered digoxin alone.

[0007a] In one aspect, the present disclosure refers to use of a therapeutically effective amount of a vesicular monoamine transporter 2 (VMAT2) inhibitor chosen from (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester and a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a hyperkinetic movement disorder in a patient, wherein the patient is also being co-administered digoxin; wherein the patient's blood is to be monitored for the digoxin exposure; and wherein the dose of digoxin is to be adjusted when the digoxin exposure in the patient's blood is increased.

[0008] These and other aspects of the ~~invention~~disclosure will be apparent upon reference to the following detailed description. To this end, various references are set forth herein which describe in more detail certain background information, procedures, compounds, and/or compositions, and are each hereby incorporated by reference in their entirety.

DETAILED DESCRIPTION

[0009] In the following description, certain specific details are set forth in order to provide a thorough understanding of various embodiments. However, one skilled in the art will understand that the invention may be practiced without these details. In other instances, well-known structures have not been shown or described in detail to avoid unnecessarily obscuring descriptions of the embodiments. Unless the context requires otherwise, throughout the specification and claims which follow, the word "comprise" and variations thereof, such as, "comprises" and "comprising" are to be construed in an open, inclusive sense, that is, as "including, but not limited to." Further, headings provided herein are for convenience only and do not interpret the scope or meaning of the claimed invention.

CLAIMS:

1. A method of administering a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+) α 3 isobutyl 9,10 dimethoxy 1,3,4,6,7,11b hexahydro 2H pyrido[2,1 a]isoquinolin 2 ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, to a patient in need thereof wherein the patient is also being administered digoxin, comprising:

administering to the patient a therapeutically effective amount of the VMAT2 inhibitor.

2. The method of claim 1, further comprising monitoring the patient for signs and symptoms of digoxin toxicity and clinical response.

3. The method of claim 1 or 2, further comprising reducing the amount of the digoxin administered to the patient based on the patient's ability to tolerate one or more digoxin exposure related adverse reactions.

4. A method of administering a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+) α 3 isobutyl 9,10 dimethoxy 1,3,4,6,7,11b hexahydro 2H pyrido[2,1 a]isoquinolin 2 ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, to a patient in need thereof, comprising:

administering to the patient a therapeutically effective amount of the VMAT2 inhibitor,

subsequently determining that the patient is to begin treatment with digoxin, and

continuing administration of the therapeutically effective amount of the VMAT2 inhibitor to the patient.

5. The method of claim 4, further comprising monitoring the patient signs and symptoms of digoxin toxicity and clinical response.

6. The method of claim 4 or 5, further comprising reducing the amount of the digoxin administered to the patient based on the patient's ability to tolerate one or more digoxin exposure related adverse reactions.

7. A method of administering a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+) α 3 isobutyl 9,10 dimethoxy 1,3,4,6,7,11b hexahydro 2H pyrido[2,1 a]isoquinolin 2 ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, to a patient in need thereof wherein the patient is also being administered digoxin, comprising:

administering a therapeutically effective amount of the VMAT2 inhibitor to the patient,

wherein the administration produces a mean digoxin C_{max} that is about 1.5 to 2.5 fold higher than the mean digoxin C_{max} for a patient who is administered digoxin alone and/or a mean digoxin $AUC_{0-\infty}$ that is about 1 to about 2 fold higher than the mean digoxin $AUC_{0-\infty}$ for a patient who is administered digoxin alone.

8. The method of any one of claims 1 to 7, further comprising informing the patient or a medical care worker that co administration of the VMAT2 inhibitor and digoxin may result in increased digoxin exposure.

9. The method of any one of claims 1 to 8, further comprising informing the patient or a medical care worker that co administration of the VMAT2 inhibitor and digoxin may result in increased risk of one or more digoxin exposure related adverse reactions.

10. The method of any one of claims 1 to 9, wherein monitoring for signs and symptoms of digoxin toxicity and clinical response comprises monitoring the serum concentration of the digoxin.

11. The method of any one of claims 1 to 9, wherein monitoring for signs and symptoms of digoxin toxicity and clinical response comprises determining whether the patient experiences one or more exposure related adverse reaction associated with serum digoxin concentration.

12. The method of any one of claims 1 to 9, wherein monitoring for signs and symptoms of digoxin toxicity and clinical response comprises monitoring efficacy of the digoxin.

13. The method of any one of claims 1 to 3, or 7 to 12, further comprising obtaining a baseline serum digoxin concentration prior to administering to the patient the therapeutically effective amount of the VMAT2 inhibitor.

14. The method of claim 13, further comprising obtaining a serum digoxin concentration after administering to the patient the therapeutically effective amount of the VMAT2 inhibitor.

15. The method of claim 14, further comprising comparing the baseline serum digoxin concentration to the serum digoxin concentration after administering to the patient the therapeutically effective amount of the VMAT2 inhibitor.

16. The method of any one of claims 1 to 15, wherein the dosage and/or frequency of administration of the digoxin is reduced.

17. The method of claim 16, wherein the dosage of digoxin is decreased.

18. The method of claim 16 or 17, wherein the frequency of administration of the digoxin is decreased.

19. The method of any one of claims 1 to 18, wherein the VMAT2 inhibitor is administered to the patient to treat a neurological or psychiatric disease or disorder.

20. The method of claim 19, wherein the neurological or psychiatric disease or disorder is a hyperkinetic movement disorder, mood disorder, bipolar disorder, schizophrenia, schizoaffective disorder, mania in mood disorder, depression in mood disorder, treatment-refractory obsessive compulsive disorder, neurological dysfunction associated with Lesch-Nyhan syndrome, agitation associated with Alzheimer's disease, Fragile X syndrome or Fragile X-associated tremor-ataxia syndrome, autism spectrum disorder, Rett syndrome, or chorea-acanthocytosis.

~~21. The method of claim 20, wherein the neurological or psychiatric disease or disorder is a hyperkinetic movement disorder.~~

~~22. The method of claim 21, wherein the hyperkinetic movement disorder is tardive dyskinesia.~~

~~23. The method of claim 21, wherein the hyperkinetic movement disorder is Tourette's syndrome.~~

~~24. The method of claim 21, wherein the hyperkinetic movement disorder is Huntington's disease.~~

~~25. The method of claim 21, wherein the hyperkinetic movement disorder is tics.~~

~~26. The method of claim 21, wherein the hyperkinetic movement disorder is chorea associated with Huntington's disease.~~

~~27. The method of claim 21, wherein the hyperkinetic movement disorder is ataxia, chorea, dystonia, Huntington's disease, myoclonus, restless leg syndrome, or tremors.~~

~~28. The method of any one of claims 1 to 27, wherein the VMAT2 inhibitor is administered orally.~~

~~29. The method of any one of claims 1 to 28, wherein the VMAT2 inhibitor is administered in the form of a tablet or capsule.~~

~~30. The method of any one of claims 1 to 29, wherein the VMAT2 inhibitor is administered with or without food.~~

~~31. The method of any one of claims 1 to 30, wherein the VMAT2 inhibitor is valbenazine or a pharmaceutically acceptable salt and/or isotopic variant thereof.~~

~~32. The method of claim 31, wherein the VMAT2 inhibitor is valbenazine or a pharmaceutically acceptable salt thereof.~~

~~33. The method of claim 32, wherein the VMAT2 inhibitor is a valbenazine tosylate salt.~~

~~34. The method of claim 33, wherein the VMAT2 inhibitor is a ditosylate salt of valbenazine.~~

~~35. The method of claim 31, wherein the VMAT2 inhibitor is an isotopic variant that is L-Valine, (*2R,3R*,11b*R*)-1,3,4,6,7,11b-hexahydro-9,10-di(methoxy-d_3)-3-(2-methylpropyl)-2*H*-benzo[*a*]quinolizin-2-yl ester or a pharmaceutically acceptable salt thereof.~~

~~36. The method of any one of claims 1 to 35, wherein the VMAT2 inhibitor is administered in an amount equivalent to between about 20 mg and about 160 mg of valbenazine free base.~~

~~37. The method of claim 36, wherein the VMAT2 inhibitor is administered in an amount equivalent to about 20 mg of valbenazine free base.~~

~~38. The method of claim 36, wherein the VMAT2 inhibitor is administered in an amount equivalent to about 40 mg of valbenazine free base.~~

~~39. The method of claim 36, wherein the VMAT2 inhibitor is administered in an amount equivalent to about 60 mg of valbenazine free base.~~

~~40. The method of claim 36, wherein the VMAT2 inhibitor is administered in an amount equivalent to about 80 mg of valbenazine free base.~~

~~41. The method of claim 36, wherein the VMAT2 inhibitor is administered in an amount equivalent to about 120 mg of valbenazine free base.~~

42. The method of any one of claims 1 to 35, wherein the VMAT2 inhibitor is administered for a first period of time in a first amount and then the amount is increased to a second amount.

43. The method of claim 42, wherein the first period of time is a week.

44. The method of claim 42 or 43, wherein the first amount is equivalent to about 40 mg of valbenazine free base.

45. The method of any one of claims 42 to 44, wherein the second amount is equivalent to about 80 mg of valbenazine free base.

46. The method of any one of claims 1 to 35, wherein the VMAT2 inhibitor is administered in an amount sufficient to achieve a maximal blood plasma concentration (C_{max}) of (+) α- DHTBZ of between about 15 ng to about 60 ng per mL plasma and a minimal blood plasma concentration (C_{min}) of (+) α- DHTBZ of at least 15 ng per mL plasma over an 8 hour period.

47. The method of any one of claims 1 to 35, wherein the VMAT2 inhibitor is administered in an amount sufficient to achieve a maximal blood plasma concentration (C_{max}) of (+) α- DHTBZ of between about 15 ng to about 60 ng per mL plasma and a minimal blood plasma concentration (C_{min}) of approximately between about at least 33%- 50% of the C_{max} over a 12 hour period.

48. The method of any one of claims 1 to 35, wherein the VMAT2 inhibitor is administered in an amount sufficient to achieve: (i) a therapeutic concentration range of about 15 ng to about 60 ng of (+) α- DHTBZ per mL plasma; and (ii) a threshold concentration of at least 15 ng (+)-α -DHTBZ per mL plasma over a period of about 8 hours to about 24 hours.

49. The method of any one of claims 1 to 35, wherein the amount of digoxin being administered is 10-90% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.

~~50. The method of any one of claims 1 to 35, wherein the amount of digoxin being administered is 20-80% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~51. The method of any one of claims 1 to 35, wherein the amount of digoxin being administered is 30-70% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~52. The method of any one of claims 1 to 35, wherein the amount of digoxin being administered is 40-60% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~53. The method of any one of claims 1 to 35, wherein the amount of digoxin being administered is 50% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor~~

~~54. The method of any one of claims 1 to 30, wherein the VMAT2 inhibitor is (+) α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof.~~

~~55. The method of claim 54, wherein the VMAT2 inhibitor is (+) α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol dihydrotetrabenazine or a pharmaceutically acceptable salt thereof.~~

~~56. The method of claim 54, wherein the VMAT2 inhibitor is an isotopic variant that is (+) α-3-isobutyl-9,10-di(methoxy-d_3)-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol or a pharmaceutically acceptable salt thereof.~~

~~57. A composition for treating a patient in need of a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+) α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant and being administered digoxin, comprising:~~

~~a therapeutically effective amount of the VMAT2 inhibitor.~~

~~58. The composition of claim 57, wherein the patient is monitored for signs and symptoms of digoxin toxicity and clinical response.~~

~~59. The composition of claim 57 or 58, characterized in that a composition comprising a reduced amount of the digoxin is administered to the patient based on the patient's ability to tolerate one or more digoxin exposure-related adverse reactions following administration of the composition comprising the therapeutically effective amount of the VMAT2 inhibitor.~~

~~60. A composition for treating a patient in need of a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+)-α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, comprising the VMAT2 inhibitor,~~

~~characterized in that the composition comprising a therapeutically effective amount of the VMAT2 inhibitor is administered to the patient subsequently determined to begin treatment with digoxin following administration of the composition comprising the therapeutically effective amount of the VMAT2 inhibitor.~~

~~61. The composition of claim 60, wherein the patient is monitored for one or more exposure-related adverse reactions.~~

~~62. The composition of any one of claim 60 or 61, characterized in that the composition comprising a reduced amount of the VMAT2 inhibitor is administered based on the patient's ability to tolerate one or more exposure-related adverse reactions following administration of the composition comprising a therapeutically effective amount of the VMAT2 inhibitor as defined in claim 4 or the composition comprising a reduced amount of the VMAT2 inhibitor as defined in claim 5.~~

~~63. A composition for treating a patient in need of a vesicular monoamine transport 2 (VMAT2) inhibitor chosen from valbenazine and (+)-α-3-isobutyl-9,10-~~

~~dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof, and being treated with digoxin, comprising:~~

~~a therapeutically effective amount of the VMAT2 inhibitor,~~

~~wherein administration of the composition produces a mean digoxin C_{max} that is about 1.5 to 2.5 fold higher than the mean digoxin C_{max} for a patient who is administered digoxin alone and/or a mean digoxin $AUC_{0-\infty}$ that is about 1 to about 2 fold higher than the mean digoxin $AUC_{0-\infty}$ for a patient who is administered digoxin alone.~~

~~64. The composition of any one of claims 57 to 63, wherein the patient or a medical care worker is informed that co-administration of the composition and digoxin may result in increased digoxin exposure.~~

~~65. The composition of any one of claims 57 to 64, wherein the patient or a medical care worker is informed that co-administration of the composition and digoxin may result in increased risk of one or more digoxin exposure-related adverse reactions.~~

~~66. The composition of any one of claims 57 to 65, wherein the serum concentration of digoxin is monitored.~~

~~67. The composition of any one of claims 57 to 66, wherein the dosage and/or frequency of administration of the digoxin is reduced.~~

~~68. The composition of claim 67, wherein the dosage of digoxin is decreased.~~

~~69. The composition of claim 67 or 68, wherein the frequency of administration of the digoxin is decreased.~~

~~70. The composition of any one of claims 57 to 69, wherein the composition is for treating a neurological or psychiatric disease or disorder.~~

~~71. The composition of claim 70, wherein the neurological or psychiatric disease or disorder is a hyperkinetic movement disorder, mood disorder, bipolar disorder, schizophrenia, schizoaffective disorder, mania in mood disorder, depression in mood disorder, treatment refractory obsessive compulsive disorder, neurological dysfunction associated with Lesch Nyhan syndrome, agitation associated with Alzheimer's disease, Fragile X syndrome or Fragile X associated tremor ataxia syndrome, autism spectrum disorder, Rett syndrome, or chorea acanthocytosis.~~

~~72. The composition of claim 71, wherein the neurological or psychiatric disease or disorder is a hyperkinetic movement disorder.~~

~~73. The composition of claim 72, wherein the hyperkinetic movement disorder is tardive dyskinesia.~~

~~74. The composition of claim 72, wherein the hyperkinetic movement disorder is Tourette's syndrome.~~

~~75. The composition of claim 72, wherein the hyperkinetic movement disorder is Huntington's disease.~~

~~76. The composition of claim 72, wherein the hyperkinetic movement disorder is tics.~~

~~77. The composition of claim 72, wherein the hyperkinetic movement disorder is chorea associated with Huntington's disease.~~

~~78. The composition of claim 72, wherein the hyperkinetic movement disorder is ataxia, chorea, dystonia, Huntington's disease, myoclonus, restless leg syndrome, or tremors.~~

~~79. The composition of any one of claims 57 to 78, characterized in that the composition is administered orally.~~

~~80. The composition of any one of claims 57 to 79, characterized in that the composition is administered in the form of a tablet or capsule.~~

~~81. The composition of any one of claims 57 to 80, characterized in that the composition is administered with or without food.~~

~~82. The composition of any one of claims 57 to 81, wherein the VMAT2 inhibitor is valbenazine or a pharmaceutically acceptable salt and/or isotopic variant thereof.~~

~~83. The composition of claim 82, wherein the VMAT2 inhibitor is valbenazine or a pharmaceutically acceptable salt thereof.~~

~~84. The composition of claim 83, wherein the VMAT2 inhibitor is a valbenazine tosylate salt.~~

~~85. The composition of claim 84, wherein the VMAT2 inhibitor is a ditosylate salt of valbenazine.~~

~~86. The composition of claim 82, wherein the VMAT2 inhibitor is an isotopic variant that is L-Valine, (*2R,3R*,11b*R*)-1,3,4,6,7,11b-hexahydro-9,10-di(methoxy-d_3)-3-(2-methylpropyl)-2*H*-benzo[*a*]quinolizin-2-yl ester or a pharmaceutically acceptable salt thereof.~~

~~87. The composition of any one of claims 57 to 86, characterized in that the composition is administered in an amount equivalent to between about 20 mg and about 160 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~88. The composition of claim 87, wherein characterized in that the composition is administered in an amount equivalent to about 20 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~89. The composition of claim 87, characterized in that the composition is administered in an amount equivalent to about 40 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~90. The composition of claim 87, characterized in that the composition is administered in an amount equivalent to about 60 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~91. The composition of claim 87, characterized in that the composition is administered in an amount equivalent to about 80 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~92. The composition of claim 87, characterized in that the composition is administered in an amount equivalent to about 120 mg of valbenazine free base of the VMAT2 inhibitor.~~

~~93. The composition of any one of claims 57 to 86, characterized in that the composition is administered for a first period of time in a first amount of the VMAT2 inhibitor and then the amount is increased to a second amount of the VMAT2 inhibitor.~~

~~94. The composition of claim 93, wherein the first period of time is a week.~~

~~95. The composition of claim 93 or 94, wherein the first amount is equivalent to about 40 mg of valbenazine free base.~~

~~96. The composition of any one of claims 93 to 95, wherein the second amount is equivalent to about 80 mg of valbenazine free base.~~

~~97. The composition of any one of claims 57 to 86, characterized in that the composition is administered in an amount sufficient to achieve a maximal blood plasma concentration (C_{max}) of (+) α- DHTBZ of between about 15 ng to about 60 ng per mL plasma and a minimal blood plasma concentration (C_{min}) of (+) α-DHTBZ of at least 15 ng per mL plasma over an 8 hour period.~~

~~98. The composition of any one of claims 57 to 86, characterized in that the composition is administered in an amount sufficient to achieve a maximal blood plasma concentration (C_{max}) of (+) α- DHTBZ of between about 15 ng to about 60 ng per mL plasma and a minimal blood plasma concentration (C_{min}) of~~

~~approximately between about at least 33% - 50% of the C_{max} over a 12 hour period.~~

~~99. The composition of any one of claims 57 to 86, characterized in that the composition is administered in an amount sufficient to achieve: (i) a therapeutic concentration range of about 15 ng to about 60 ng of (+) α- DHTBZ per mL plasma; and (ii) a threshold concentration of at least 15 ng (+) α- DHTBZ per mL plasma over a period of about 8 hours to about 24 hours.~~

~~100. The composition of any one of claims 57 to 86, characterized in that the amount of digoxin being administered is 10-90% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~101. The composition of any one of claims 57 to 86, characterized in that the amount of digoxin being administered is 20-80% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~102. The composition of any one of claims 57 to 86, characterized in that the amount of digoxin being administered is 30-70% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~103. The composition of any one of claims 57 to 86, characterized in that the amount of digoxin being administered is 40-60% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor.~~

~~104. The composition of any one of claims 57 to 86, characterized in that the amount of digoxin being administered is 50% less than the amount that would be administered to a patient who is not also being administered a VMAT2 inhibitor~~

~~105. The composition of any one of claims 57 to 81, characterized in that the VMAT2 inhibitor is (+)-α-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol, or a pharmaceutically acceptable salt and/or isotopic variant thereof.~~

~~106. The composition of claim 105, wherein the VMAT2 inhibitor is (+) α 3 isobutyl 9,10 dimethoxy 1,3,4,6,7,11b hexahydro 2H pyrido[2,1 a]isoquinolin 2 ol dihydrotetrabenazine or a pharmaceutically acceptable salt thereof.~~

~~107. The composition of claim 105, wherein the VMAT2 inhibitor is an isotopic variant that is (+) α 3 isobutyl 9,10 di(methoxy d_3) 1,3,4,6,7,11b hexahydro 2H pyrido[2,1 a]isoquinolin 2 ol or a pharmaceutically acceptable salt thereof.~~

1. Use of a therapeutically effective amount of a vesicular monoamine transporter 2 (VMAT2) inhibitor chosen from (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester and a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a hyperkinetic movement disorder in a patient, wherein the patient is also being co-administered digoxin;

wherein the patient's blood is to be monitored for the digoxin exposure; and

wherein the dose of digoxin is to be adjusted when the digoxin exposure in the patient's blood is increased.

2. The use of claim 1, wherein adjustment of the dose of digoxin comprises reduction of the dose of digoxin.

3. The use of claim 1 or 2, wherein the digoxin exposure is to be measured as the area under the plasma concentration versus time curve from 0 hours extrapolated to infinity ($AUC_{0-\infty}$) or measured as the maximum observed blood plasma concentration (C_{max}) at the time of maximum plasma concentration (t_{max}).

4. The use of claim 3, further wherein the subject is to be monitored for one or more exposure-related adverse reactions.

5. The use of claim 4, wherein the one or more exposure-related adverse reactions is selected from headache, anxiety, insomnia, diarrhea, restlessness, and abnormal dreams.

6. The use of any one of claims 1 to 5, further wherein a baseline serum digoxin concentration is to be obtained prior to administration to the patient the therapeutically effective amount of the VMAT2 inhibitor.

7. The use of any one of claims 1 to 6, wherein the dosage and/or frequency of administration of the digoxin is to be reduced.

8. The use of any one of claims 1 to 7, wherein the VMAT2 inhibitor is a salt of (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester.

9. The use of any one of claims 1 to 8, wherein the VMAT2 inhibitor is (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester ditosylate.

10. The use of any one of claims 1 to 9, wherein the hyperkinetic movement disorder is tardive dyskinesia.

11. The use of any one of claims 1 to 9, wherein the hyperkinetic movement disorder is Tourette's syndrome.

12. The use of any one of claims 1 to 9, wherein the hyperkinetic movement disorder is Huntington's disease.

13. The use of any one of claims 1 to 9, wherein the hyperkinetic movement disorder is tics.

14. The use of any one of claims 1 to 9, wherein the hyperkinetic movement disorder is chorea.

15. The use of claim 14, wherein the hyperkinetic movement disorder is chorea associated with Huntington's disease.

16. The use of any one of claims 1 to 15, wherein the therapeutically effective amount is an amount equivalent to about 40 mg as measured by (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily for one week, and an amount equivalent to about 80 mg as measured by (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily after one week.

17. The use of any one of claims 1 to 15, wherein the therapeutically effective amount is an amount equivalent to about 40 mg as measured by (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.

18. The use of any one of claims 1 to 15, wherein the therapeutically effective amount is an amount equivalent to about 60 mg as measured by (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.

19. The use of any one of claims 1 to 15, wherein the therapeutically effective amount is an amount equivalent to about 80 mg as measured by (S)-2-amino-3-methyl-butyric acid (2R,3R,11bR)-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-yl ester free base once daily.