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 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. 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.