[0004] Accordingly, there is a need for alternative therapies that can be used for the treatment of depression, anxiety and post-traumatic stress disorder that may address one or more of the limitations associated with current treatments.

Summary

[0004a] In an aspect, there is provided a pharmaceutical composition comprising flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are present in a ratio of from about 25:1 to about 10:1 by weight.

[0004b] In another aspect, there is provided the use of flumazenil or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with naltrexone or a pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

[0004c] In another aspect, there is provided the use of naltrexone or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with flumazenil or a pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

[0004d] In another aspect, there is provided the use of a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating depression and/or anxiety and/or post-traumatic stress disorder, wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

[0004e] In another aspect, there is provided a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, for use in the treatment of

depression and/or anxiety and/or post-traumatic stress disorder, wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

[0005] The present disclosure~~invention~~ is predicated at least in part on the discovery that the combination of microdose flumazenil and microdose naltrexone may be useful in the treatment of conditions such as depression, anxiety and PTSD.

[0006] In one ~~aspect~~ example of the present ~~invention~~disclosure, there is provided a pharmaceutical composition comprising flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are present in a ratio of from about 300:1 to about 2:1 by weight.

[0007] In another ~~aspect~~example of the present disclosure~~invention~~, there is provided a method for treating depression comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio of from about 300:1 to about 2:1 by weight.

[0008] In a further ~~aspect~~ example of the present disclosure~~invention~~, there is provided a method for treating anxiety comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio of from about 300:1 to about 2:1 by weight.

[0009] In a further ~~aspect~~example of the present disclosure~~invention~~, there is provided a method for treating post-traumatic stress disorder comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio of from about 300:1 to about 2:1 by weight.

The claims defining the invention are as follows:

1. A pharmaceutical composition comprising flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are present in a ratio of from about 25:1 to about 10:1 by weight.

2. The pharmaceutical composition of claim 1, wherein the composition is in the form of a single dosage unit.

3. The pharmaceutical composition of claim 2, wherein the single dosage unit is formulated for administration over about 4 days.

4. The pharmaceutical composition of claim 2 or 3, wherein the single dosage unit comprises flumazenil in an amount to provide a daily dose ranging from about 250 to about 7,500 micrograms.

5. The pharmaceutical composition of any one of claims 2 to 4, wherein the single dosage unit comprises naltrexone in an amount to provide a daily dose ranging from about 25 to about 1,000 micrograms.

6. The pharmaceutical composition of any one of claims 2 to 5, wherein the flumazenil is present in the single dosage unit in an amount ranging from about 1,000 to about 30,000 micrograms.

7. The pharmaceutical composition of any one of claims 2 to 6, wherein the naltrexone is present in the single dosage unit in an amount ranging from about 100 to about 4,000 micrograms.

8. The pharmaceutical composition of any one of claims 1 to 7, wherein the composition is formulated for subcutaneous administration.

9. The pharmaceutical composition of any one of claims 1 to 7, wherein the composition is formulated for nasal delivery.

~~10. A method for treating depression comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio ranging from about 25:1 to about 10:1 by weight.~~

~~11. A method for treating anxiety comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio ranging from about 25:1 to about 10:1 by weight.~~

~~12. A method for treating post-traumatic stress disorder comprising administering to a patient in need thereof a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, wherein the flumazenil and naltrexone are administered in a ratio ranging from about 25:1 to about 10:1 by weight.~~

10. Use of flumazenil or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with naltrexone or a pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

11. Use of naltrexone or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with flumazenil or a pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

12. Use of a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating depression and/or anxiety and/or post-traumatic stress disorder, wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

13. The ~~method of any one~~use of claims 10 to 12, wherein one or more of the following applies:

i) the flumazenil is to be administered to provide a daily dose ranging from about 250 to about 7,500 micrograms;

ii) the naltrexone is to be administered to provide a daily dose ranging from about 25 to about 1,000 micrograms;

iii) the flumazenil is to be administered to provide a total dose over the course of the treatment ranging from about 4,000 to about 120,000 micrograms; and

iv) the naltrexone is to be administered to provide a total dose over the course of the treatment ranging from about 400 to about 16,000 micrograms

14. The ~~method~~use of any one of claims 10 to 13, wherein the flumazenil and naltrexone are to be administered in a single composition.

15. The ~~method~~use of any one of claims 10 to 14, wherein the combination of flumazenil and naltrexone is to be administered by continuous dosing.

16. The use~~method~~ of any one of claims 10 to 15, wherein the combination of flumazenil and naltrexone is to be administered by interrupted dosing.

~~17. Use of a combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, for treating depression and/or anxiety and/or post-traumatic stress disorder, wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.~~

~~18.~~17. A combination of flumazenil and naltrexone, or pharmaceutically acceptable salts thereof, for use in the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.

~~19. Use of flumazenil or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with naltrexone or a~~

~~pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.~~

~~20. Use of naltrexone or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of depression and/or anxiety and/or post-traumatic stress disorder, wherein the medicament is adapted for use in combination with flumazenil or a pharmaceutically acceptable salt thereof and wherein the flumazenil and naltrexone are in a ratio of from about 25:1 to about 10:1 by weight.~~

~~21.~~18. A kit comprising one or more pharmaceutical compositions according to any one of claims 1 to 9, and a delivery device.