SUMMARY OF THE DISCLOSURE

[0009] The present disclosure relates to methods of treating schizophrenia or bipolar disorder in a patient comprising subcutaneously administering to the patient, with a frequency of no more than once per 21 days, a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt thereof. The sustained-release pharmaceutical dosage forms of the disclosure provide a therapeutically effective dose of olanzapine for a period of at least 21 days. In addition, the disclosed methods are performed without a need for monitoring for PDSS.

[0010] The present disclosure also relates to methods of administering between about 150 mg and about 900 mg of olanzapine, or a pharmaceutically acceptable salt thereof, to a patient. These methods comprise subcutaneously administering to the patient a sustained-release olanzapine pharmaceutical dosage form at a frequency of no more than one per 21 days. According to these methods, the per-injection risk of PDSS being observed in the patient following the administration is less than 0.07% and/or the per-patient risk of PDSS being observed in the patient following the administration is less than 1.4%.

[0010a] In one aspect, the present disclosure relates to the use of a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt thereof, and at least one biodegradable polymer, wherein the at least one biodegradable polymer is a poly(lactide), poly(glycolide), poly(lactide-co-glycolide), poly-1-lactic acid, poly-d-lactic acid, poly(glycolic acid), copolymers of the foregoing, poly(aliphatic carboxylic acids), copolyoxalates, polycaprolactone, polydioxanone, poly(ortho carbonates), poly(acetals), poly(lactic acid-caprolactone), polyorthoesters, poly(glycolic acid-captolactone), poly(amino acid), polyesteramide, polyanhydrides, polyphosphazines, poly(alkylene alkylate), biodegradable polyurethane, polyvinylpyrrolidone, polyalkanoic acid, polyethylene glycol, copolymer of polyethylene glycol and polyorthoester, albumin, chitosan, casein, waxes or blends or copolymers thereof, in the manufacture of a medicament for treating schizophrenia or bipolar disorder in a patient, wherein the medicament is to be administered by subcutaneous injection to the patient, at a frequency of no more than once per 21 days; wherein said dosage form provides a therapeutically effective dose of olanzapine for a period of at least 21 days; and wherein said patient is not monitored for post-injection delirium/sedation syndrome (PDSS).

[0010b] In another aspect, the present disclosure relates to the use of a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt thereof, and at least one biodegradable polymer, wherein the at least one biodegradable polymer is a

poly(lactide), poly(glycolide), poly(lactide-co-glycolide), poly-1-lactic acid, poly-d-lactic acid, poly(glycolic acid), copolymers of the foregoing, poly(aliphatic carboxylic acids), copolyoxalates, polycaprolactone, polydioxanone, poly(ortho carbonates), poly(acetals), poly(lactic acid-caprolactone), polyorthoesters, poly(glycolic acid-captolactone), poly(amino acid), polyesteramide, polyanhydrides, polyphosphazines, poly(alkylene alkylate), biodegradable polyurethane, polyvinylpyrrolidone, polyalkanoic acid, polyethylene glycol, copolymer of polyethylene glycol and polyorthoester, albumin, chitosan, casein, waxes or blends or copolymers thereof, in the manufacture of a medicament for treating schizophrenia or bipolar disorder, wherein between 150 mg and 900 mg of olanzapine, or a pharmaceutically acceptable salt thereof, is to be administered to a patient, wherein the medicament is to be administered by subcutaneous injection to the patient at a frequency of no more than once per 21 days; wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.07% and/or the per-patient risk of PDSS being observed in the patient following the administration is less than 1.4%.

BRIEF DESCRIPTION OF THE FIGURES

[0011] Fig.1 - is a graph that demonstrates the percentage of olanzapine released over time from different formulations.

[0012] Fig.2 - is a graph that demonstrates the pharmacokinetic profiles in dogs following subcutaneous administration of the sustained release olanzapine formulations and IM administration of olanzapine pamoate.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0013] Reference will now be made to the exemplary embodiments and specific language will be used herein to describe the same. It will nevertheless be understood that no limitation of the scope of the invention is thereby intended. Alterations and further modifications of the inventive features illustrated herein, and additional applications of the principles of the inventions as illustrated herein, which would occur to one skilled in the relevant art and having possession of this disclosure, are to be considered within the scope of the invention.

[0014] The present disclosure is directed to methods of treating schizophrenia or bipolar disorder in a patient. These methods comprise subcutaneously administering to the patient, with a frequency of no more than once per 21 days, a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt of olanzapine.

CLAIMS:

1. Use of a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt thereof, and at least one biodegradable polymer, wherein the at least one biodegradable polymer is a poly(lactide), poly(glycolide), poly(lactide-co-glycolide), poly-1-lactic acid, poly-d-lactic acid, poly(glycolic acid), copolymers of the foregoing, poly(aliphatic carboxylic acids), copolyoxalates, polycaprolactone, polydioxanone, poly(ortho carbonates), poly(acetals), poly(lactic acid-caprolactone), polyorthoesters, poly(glycolic acid-captolactone), poly(amino acid), polyesteramide, polyanhydrides, polyphosphazines, poly(alkylene alkylate), biodegradable polyurethane, polyvinylpyrrolidone, polyalkanoic acid, polyethylene glycol, copolymer of polyethylene glycol and polyorthoester, albumin, chitosan, casein, waxes or blends or copolymers thereof, in the manufacture of a medicament for treating schizophrenia or bipolar disorder in a patient, wherein the medicament is to be administered by subcutaneous injection to the patient, at a frequency of no more than once per 21 days; wherein said dosage form provides a therapeutically effective dose of olanzapine for a period of at least 21 days; and wherein said patient is not monitored for post-injection delirium/sedation syndrome (PDSS).

2. The use of claim 1, wherein the pharmaceutical dosage form comprises olanzapine.

3. The use of claim 1, wherein the pharmaceutical dosage form comprises a pharmaceutically acceptable olanzapine salt.

4. The use of any one of the preceding claims, wherein the pharmaceutical dosage form comprises between 150 mg and 900 mg of olanzapine or a pharmaceutically acceptable salt thereof.

5. The use of claim 4, wherein the pharmaceutical dosage form comprises between 300 mg and 600 mg of olanzapine or a pharmaceutically acceptable salt thereof.

6. The use of claim 4, wherein the pharmaceutical dosage form comprises 300 mg of olanzapine or a pharmaceutically acceptable salt thereof.

7. The use of claim 4, wherein the pharmaceutical dosage form comprises 405 mg olanzapine or a pharmaceutically acceptable salt thereof.

8. The use of claim 4, wherein the pharmaceutical dosage form comprises 600 mg olanzapine or a pharmaceutically acceptable salt thereof.

9. The use of any one of the preceding claims, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for at least 30 days.

10. The use of claim 9, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for at least 60 days.

11. The use of claim 9, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for 90 days.

12. Use of a sustained-release pharmaceutical dosage form comprising olanzapine, or a pharmaceutically acceptable salt thereof, and at least one biodegradable polymer, wherein the at least one biodegradable polymer is a poly(lactide), poly(glycolide), poly(lactide-co-glycolide), poly-1-lactic acid, poly-d-lactic acid, poly(glycolic acid), copolymers of the foregoing, poly(aliphatic carboxylic acids), copolyoxalates, polycaprolactone, polydioxanone, poly(ortho carbonates), poly(acetals), poly(lactic acid-caprolactone), polyorthoesters, poly(glycolic acid-captolactone), poly(amino acid), polyesteramide, polyanhydrides,

polyphosphazines, poly(alkylene alkylate), biodegradable polyurethane, polyvinylpyrrolidone, polyalkanoic acid, polyethylene glycol, copolymer of polyethylene glycol and polyorthoester, albumin, chitosan, casein, waxes or blends or copolymers thereof, in the manufacture of a medicament for treating schizophrenia or bipolar disorder in a patient, wherein between 150 mg and 900 mg of olanzapine, or a pharmaceutically acceptable salt thereof, is to be administered to a patient, wherein the medicament is to be administered by subcutaneous injection

to the patient at a frequency of no more than once per 21 days;

wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.07% and/or the per-patient risk of PDSS being observed in the patient following the administration is less than 1.4%.

13. The use of claim 12, wherein the frequency of administration is no more than once per month.

14. The use of claim 13, wherein the frequency of administration is no more than once every two months.

15. The use of any one of claims 12 to 14, wherein the pharmaceutical dosage form comprises between 300 mg and 600 mg of olanzapine or a pharmaceutically acceptable salt thereof.

16. The use of claim 15, wherein the pharmaceutical dosage form comprises 300 mg of olanzapine or a pharmaceutically acceptable salt thereof that is equivalent to 300 mg of olanzapine.

17. The use of claim 15, wherein the pharmaceutical dosage form comprises 405 mg olanzapine or a pharmaceutically acceptable salt thereof that is equivalent to 405 mg of olanzapine.

18. The use of claim 15, wherein the pharmaceutical dosage form comprises 600 mg olanzapine or a pharmaceutically acceptable salt thereof that is equivalent to 600 mg of olanzapine.

19. The use of any one of claims 12 to 18, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for at least 30 days.

20. The use of claim 19, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for at least 60 days.

21. The use of claim 20, wherein the pharmaceutical dosage form provides a therapeutically effective dose of olanzapine for 90 days.

22. The use of any one of claims 12 to 18, wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.01%.

23. The use of claim 22, wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.005%.

24. The use of claim 22, wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.001%.

25. The use of claim 22, wherein the per-injection risk of PDSS being observed in the patient following the administration is less than 0.0005%.

26. The use of claim 22, wherein the per-injection risk of PDSS being observed in the patient following the administration is 0%.

27. The use of any one of claims 12 to 18, wherein the per-patient risk of PDSS being observed in the patient is less than 1.4%.

28. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 1%.

29. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 0.75%.

30. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 0.5%.

31. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 0.25%.

32. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 0.1%.

33. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is less than 0.05%.

34. The use of claim 27, wherein the per-patient risk of PDSS being observed in the patient is 0%.

35. The use of any one of the preceding claims, wherein the sustained-release olanzapine pharmaceutical dosage form releases less than 40 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

36. The use of claim 35, wherein the pharmaceutical dosage form releases less than 30 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour

37. The use of claim 35, wherein the pharmaceutical dosage form releases less than 20 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

38. The use of claim 35, wherein the pharmaceutical dosage form releases less than 10 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

39. The use of claim 35, wherein the pharmaceutical dosage form releases less than 5 wt% of

the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

40. The use of claim 35, wherein the pharmaceutical dosage form releases less than 3 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

41. The use of claim 35, wherein the pharmaceutical dosage form releases less than 1 wt% of the olanzapine, based on the weight of the administered olanzapine, into human plasma at 1 hour.

42. The use of any one of claims 12 to 41, wherein the patient has been diagnosed with schizophrenia.

43. The use of any one of claims 12 to 41, wherein the patient has been diagnosed with bipolar disorder.