alleviating excessive daytime sleepiness and fatigue in patients with Parkinson's disease, improving myoclonus and essential tremor, and reducing tardive dyskinesia and bipolar disorder (See Ondo et al., 2008, Arch. Neural. 65: 1337; Frucht et al., 2005, Neurology 65: 1967; Berner, 2008, J. Clin. Psychiatry 69: 862).

[0004] Xyrem®, for use with patients with narcolepsy, is a chronically used product that requires high dose strengths of the drug. The amount of sodium intake from the drug significantly increases the dietary sodium intake for patients, which is undesirable for all patients, and especially those with cardiometabolic risk, such as patients with heart failure, hypertension, or impaired renal function. Thus, there is a need in the art for oxybate compositions and treatment methods that provide reduced patient sodium intake compared to Xyrem®.

SUMMARY

[0004a] In an aspect of the present disclosure, there is provided a use of a mixed salt oxybate composition in the manufacture of a medicament for treating a patient who has cataplexy or excessive daytime sleepiness with narcolepsy, wherein the patient was being administered sodium oxybate and is to be switched to administration with the mixed salt oxybate composition, wherein the amount of the sodium oxybate and the mixed salt oxybate are within 10% on an oxybate dosing strength basis.

[0004b] In another aspect of the present disclosure, there is provided a use of a mixed salt oxybate in the manufacture of a medicament for treating cataplexy or excessive daytime sleepiness in patients with narcolepsy, wherein

a patient who is to be administered sodium oxybate is switched to the mixed salt oxybate, and

wherein the amount of sodium oxybate and mixed salt oxybate are within 5% on an oxybate dosing strength basis.

[0004c] In a further aspect of the present disclosure, there is provided a use of a mixed salt oxybate composition in the manufacture of a medicament for substituting a mixed salt oxybate composition for a sodium oxybate composition in a patient treated for cataplexy or excessive daytime sleepiness in patients with narcolepsy, wherein:

a. a patient that was treated with a therapeutically effective amount of sodium oxybate is determined to be sensitive to high sodium intake; and

b. if the patient is sensitive to high sodium intake, a mixed salt oxybate is to be administered to the patient,

wherein the amount of the sodium oxybate and mixed salt oxybate are the same on an oxybate dosing strength basis.

[0005] In one example, the present disclosure provides methods of substituting, exchanging, changing or switching a mixed salt oxybate composition for a sodium oxybate composition in a patient treated with sodium oxybate (such as a patient treated for cataplexy, excessive daytime sleepiness in patients with narcolepsy, or idiopathic hypersomnia), wherein the amount of the sodium oxybate and mixed salt oxybate are the same on an oxybate dosing strength basis.

[0006] In some examples, the mixed salt oxybate comprises about 8% mol. equiv. of sodium oxybate, about 23% mol. equiv. of potassium oxybate, about 21% mol. equiv. of magnesium oxybate and about 48% mol. equiv. of calcium oxybate.

[0007] In one example, the present disclosure provides for switching a patient who is administered sodium oxybate for the treatment of cataplexy or excessive daytime sleepiness in patients with narcolepsy to a mixed salt oxybate composition, the method comprising:

administering a therapeutically effective amount a mixed salt oxybate to the patient, wherein the amount of sodium oxybate and the mixed salt oxybate are the same on an oxybate dosing strength basis.

[0008] In one example, the present disclosure provides for treating cataplexy or excessive daytime sleepiness in patients with narcolepsy, the method comprising:

switching the dose of a patient who is administered sodium oxybate to a mixed salt oxybate,

wherein the switching comprises administering a therapeutically effective amount of the mixed salt oxybate to the patient and wherein the amount of sodium oxybate and mixed salt oxybate are the same on an oxybate dosing strength basis.

[0009] In some examples, about 0.5 g-9 g of the mixed salt oxybate is administered per day. In some examples, about 0.5 g of the mixed salt oxybate is administered per day. In some examples, about 0.25 g of the mixed salt oxybate is administered twice per day. In some examples, about 1.0 g of the mixed salt oxybate is administered per day. In some examples, about 0.5 g of the mixed salt oxybate is administered twice per day. In some examples, about 1.5 g of the mixed salt oxybate is administered per day. In some examples, about 0.75 g of the mixed salt oxybate is administered twice per day. In some examples, about 2.0 g of the mixed salt oxybate is administered per day. In some examples, about 1.0 g of the mixed salt oxybate is administered twice per day. In some examples, about 2.5 g of the mixed salt oxybate is administered per day. In some examples, about 1.25 g of the mixed salt oxybate is administered twice per day. In some examples, about 3.0 g of the mixed salt oxybate is administered per day. In some examples, about 1.5 g of the mixed salt oxybate is administered twice per day. In some examples, about 3.5 g of the mixed salt oxybate is administered per day. In some examples, about 1.75 g of the mixed salt oxybate is administered twice per day. In some examples, about 4.0 g of the mixed salt oxybate is administered per day. In some examples, about 2.0 g of the mixed salt oxybate is administered twice per day. In some examples, about 4.5 g of the mixed salt oxybate is administered per day. In some examples, about 2.25 g of the mixed salt oxybate is administered twice per day. In some examples, about 6 g of the mixed salt oxybate is administered per day. In some examples, about 3 g of the mixed salt oxybate is administered twice per day. In some examples, about 7.5 g of the mixed salt oxybate is administered per day. In some examples, about 3.75 g of the mixed salt oxybate is administered twice per day. In some examples, about 9 g of the mixed salt oxybate is administered per day. In some examples, about 4.5 g of the mixed salt oxybate is administered twice per day.

[0010] In some examples, the mixed salt oxybate is administered at bedtime. In some examples, the mixed salt oxybate is administered at bedtime and about 2.5 h-4 h after the bedtime administration.

[0011] In some examples, mixed salt oxybate is in a liquid. In some examples, the concentration of the mixed salt in the liquid is about 0.5 g/mL.

[0012] In some examples, the patient is treated for cataplexy. In some examples, the patient is treated for excessive daytime sleepiness in patients with narcolepsy. In some examples, the patient is treated for idiopathic hypersomnia.

BRIEF DESCRIPTION OF THE FIGURES

[0013] FIG. 1 shows mean plasma oxybate concentration-time profiles for Xyrem and JZP-258 under fasted and fed conditions from patients in Example 1, Study 1.

[0014] FIG. 2 shows mean plasma oxybate concentration-time profiles for Xyrem and JZP-258 under fasted and fed conditions from patients in Example 1, Study 2.

[0015] FIG. 3 shows the disposition of subjects in the study of Example 2 evaluating the efficacy of JZP-258. Patients entered the open-label optimized treatment and titration period, where the dose of JZP-258 could be adjusted if needed to provide a stable, tolerable, and effective dose.

Definitions

[0016] Throughout this disclosure, various patents, patent applications and publications are referenced. The disclosures of these patents, patent applications and publications in their entireties are incorporated into this disclosure by reference for all purposes in order to more fully describe the state of the art as known to those skilled therein as of the date of this disclosure. This disclosure will govern in the instance that there is any inconsistency between the patents, patent applications and publications cited and this disclosure.

[0017] For convenience, certain terms employed in the specification, examples and claims are collected here. Unless defined otherwise, all technical and scientific terms used in this disclosure have the same meanings as commonly understood by one of ordinary skill in the art to which this disclosure belongs.

[0018] The term “about” when immediately preceding a numerical value means a range (e.g., plus or minus 10% of that value). For example, “about 50” can mean 45 to 55, “about 25,000” can mean 22,500 to 27,500, etc., unless the context of the disclosure

CLAIMS

What is claimed:

1. Use of a mixed salt oxybate composition in the manufacture of a medicament for treating a patient who has cataplexy or excessive daytime sleepiness with narcolepsy, wherein the patient was being administered sodium oxybate and is to be switched to administration with the mixed salt oxybate composition, wherein the amount of the sodium oxybate and the mixed salt oxybate are within 10% on an oxybate dosing strength basis.

2. The use of claim 1, wherein the mixed salt oxybate comprises sodium oxybate, potassium oxybate, magnesium oxybate and calcium oxybate, and wherein the mixed salt oxybate comprises about 5%-40% sodium oxybate (wt/wt%).

3. The use of claim 2, wherein the mixed salt oxybate comprises about 5%-40% of sodium oxybate (wt/wt%), about 10%-40% of potassium oxybate (wt/wt%), about 5%-30% of magnesium oxybate (wt/wt%), and about 20%-80% of calcium oxybate (wt/wt%).

4. The use of claim 3, wherein the mixed salt oxybate comprises about 8% mol. equiv. of sodium oxybate, about 23% mol. equiv. of potassium oxybate, about 21% mol. equiv. of magnesium oxybate and about 48% mol. equiv. calcium oxybate.

5. The use of any one of claims 1-4, wherein the patient is sensitive to high sodium intake.

6. The use of any one of claims 1-5, wherein the patient is in heart failure.

7. The use of any one of claims 1-5, wherein the patient is hypertensive.

8. The use of any one of claims 1-5, wherein the patient has renal impairment.

9. The use of any one of claims 1-5, wherein the patient is at risk for stroke.

10. The use of any one of claims 1-9, wherein about 0.25 g-10.0 g, 2.0 g-10.0 g; about 3.0 g-9.5 g; or about 4.5 g-9.0 g of the mixed salt oxybate is to be administered per day.

11. The use of claim 10, wherein the mixed salt oxybate is to be administered twice per day.

12. The use of claim 10, wherein the mixed salt oxybate is to be administered once per day.

13. The use of any one of claims 1-12, wherein about 4.5 g of the mixed salt oxybate is to be administered per day.

14. The use of claim 13, wherein about 2.25 g of the mixed salt oxybate is to be administered twice per day.

15. The use of any one of claims 1-12, wherein about 6.0 g of the mixed salt oxybate is to be administered per day.

16. The use of claim 15, wherein about 3.0 g of the mixed salt oxybate is to be administered twice per day.

17. The use of any one of claims 1-12, wherein about 7.5 g of the mixed salt oxybate is to be administered per day.

18. The use of claim 17, wherein about 3.75 g of the mixed salt oxybate is to be administered twice per day.

19. The use of any one of claims 1-12, wherein about 9.0 g of the mixed salt oxybate is to be administered per day.

20. The use of claim 19, wherein about 4.5 g of the mixed salt oxybate is to be administered twice per day.

21. The use of any one of claims 1-20, wherein the mixed salt oxybate composition is a liquid.

22. The use of claim 21, wherein the concentration of the mixed salt oxybate in the liquid is from 350 mg/ml-650 mg/ml, or about 450 mg/ml-550 mg/ml.

23. The use of claim 21, wherein the concentration of the mixed salt oxybate in the liquid is about 0.5 g/mL.

24. The use of any one of claims 1-23, wherein the patient is treated for cataplexy.

25. The use of any one of claims 1-23, wherein the patient is treated for excessive daytime sleepiness in patients with narcolepsy.

26. The use of any one of claims 1-25, wherein the mixed salt oxybate is to be administered at bedtime.

27. The use of any one of claims 1-26 wherein the mixed salt oxybate is to be administered at bedtime and about 2.5 h-4 h after the bedtime administration.

28. Use of a mixed salt oxybate in the manufacture of a medicament for treating cataplexy or excessive daytime sleepiness in patients with narcolepsy, wherein
    a patient who is to be administered sodium oxybate is switched to the mixed salt oxybate, and
    wherein the amount of sodium oxybate and mixed salt oxybate are within 5% on an oxybate dosing strength basis.

29. The use of claim 28, wherein the mixed salt oxybate comprises sodium oxybate, potassium oxybate, magnesium oxybate and calcium oxybate, and wherein the mixed salt oxybate comprises about 5%-40% sodium oxybate (wt/wt%).

30. The use of claim 29, wherein the mixed salt oxybate comprises about 5%-40% of sodium oxybate (wt/wt%), about 10%-40% of potassium oxybate (wt/wt%), about 5%-30% of magnesium oxybate (wt/wt%), and about 20%-80% of calcium oxybate (wt/wt%).

31. The use of claim 30, wherein the mixed salt oxybate comprises about 8% mol. equiv. of sodium oxybate, about 23% mol. equiv. of potassium oxybate, about 21% mol. equiv. of magnesium oxybate and about 48% mol. equiv. of calcium oxybate.

32. The use of any one of claims 28-31, wherein the patient is sensitive to high sodium intake.

33. The use of any one of claims 28-32, wherein the patient is in heart failure.

34. The use of any one of claims 28-32, wherein the patient is hypertensive.

35. The use of any one of claims 28-32, wherein the patient has renal impairment.

36. The use of any one of claims 28-32, wherein the patient is at risk for stroke.

37. The use of any one of claims 28-36, wherein about 2.0 g-10.0 g; about 3.0 g-9.5 g; or about 4.5 g-9.0 g of the mixed salt oxybate is to be administered per day.

38. The use of claim 37, wherein the mixed salt oxybate is to be administered twice per day.

39. The use of claim 37, wherein the mixed salt oxybate is to be administered once per day.

40. The use of any one of claims 28-39, wherein about 4.5 g of the mixed salt oxybate is to be administered per day.

41. The use of claim 40, wherein about 2.25 g of the mixed salt oxybate is to be administered twice per day.

42. The use of any one of claims 28-39, wherein about 6 g of the mixed salt oxybate is to be administered per day.

43. The use of claim 42, wherein about 3.0 g of the mixed salt oxybate is to be administered twice per day.

44. The use of any one of claims 28-39, wherein about 7.5 g of the mixed salt oxybate is to be administered per day.

45. The use of claim 44, wherein about 3.75 g of the mixed salt oxybate is to be administered twice per day.

46. The use of any one of claims 28-39, wherein about 9.0 g of the mixed salt oxybate is to be administered per day.

47. The use of claim 46, wherein about 4.5 g of the mixed salt oxybate is to be administered twice per day.

48. The use of any one of claims 28-47, wherein the mixed salt oxybate composition is a liquid.

49. The use of claim 48, wherein the concentration of the mixed salt oxybate in the liquid is from 350 mg/ml-650 mg/ml, or about 450 mg/ml-550 mg/ml.

50. The use of claim 48, wherein the concentration of the mixed salt oxybate in the liquid is about 0.5 g/mL.

51. The use of any one of claims 28-50, wherein the patient is treated for cataplexy.

52. The use of any one of claims 28-50, wherein the patient is treated for excessive daytime sleepiness in patients with narcolepsy.

53. The use of any one of claims 28-52, wherein the mixed salt oxybate is to be administered at bedtime.

54. The use of any one of claims 28-53, wherein the mixed salt oxybate is to be administered at bedtime and about 2.5 h-4 h after the bedtime administration.

55. Use of a mixed salt oxybate composition in the manufacture of a medicament for substituting a mixed salt oxybate composition for a sodium oxybate composition in a patient treated for cataplexy or excessive daytime sleepiness in patients with narcolepsy, wherein:
    a. a patient that was treated with a therapeutically effective amount of sodium oxybate is determined to be sensitive to high sodium intake; and
    b. if the patient is sensitive to high sodium intake, a mixed salt oxybate is to be administered to the patient,
    wherein the amount of the sodium oxybate and mixed salt oxybate are the same on an oxybate dosing strength basis.

56. The use of claim 55, wherein the mixed salt oxybate comprises sodium oxybate, potassium oxybate, magnesium oxybate and calcium oxybate, and wherein the mixed salt oxybate comprises about 5%-40% sodium oxybate (wt/wt%).

57. The use of claim 56, wherein the mixed salt oxybate comprises about 5%-40% of sodium oxybate (wt/wt%), about 10%-40% of potassium oxybate (wt/wt%), about 5%-30% of magnesium oxybate (wt/wt%), and about 20%-80% of calcium oxybate (wt/wt%).

58. The use of claim 57, wherein the mixed salt oxybate comprises about 8% mol. equiv. of sodium oxybate, about 23% mol. equiv. of potassium oxybate, about 21% mol. equiv. of magnesium oxybate and about 48% mol. equiv. of calcium oxybate.

59. The use of any one of claims 55-58, wherein the patient is in heart failure.

60. The use of any one of claims 55-58, wherein the patient is hypertensive.

61. The use of any one of claims 55-58, wherein the patient has renal impairment.

62. The use of any one of claims 55-58, wherein the patient is at risk for stroke.

63. The use of any one of claims 55-62, wherein about 2.0 g-10.0 g; about 3.0 g-9.5 g; or about 4.5 g-9.0 g of the mixed salt oxybate is to be administered per day.

64. The use of claim 63, wherein the mixed salt oxybate is to be administered twice per day.

65. The use of claim 63, wherein the mixed salt oxybate is to be administered once per day.

66. The use of any one of claims 55-65, wherein about 4.5 g of the mixed salt oxybate is to be administered per day.

67. The use of claim 66, wherein about 2.25 g of the mixed salt oxybate is to be administered twice per day.

68. The use of any one of claims 55-65, wherein about 6.0 g of the mixed salt oxybate is to be administered per day.

69. The use of claim 68, wherein about 3 g of the mixed salt oxybate is to be administered twice per day.

70. The use of any one of claims 55-65, wherein about 7.5 g of the mixed salt oxybate is to be administered per day.

71. The use of claim 70, wherein about 3.75 g of the mixed salt oxybate is to be administered twice per day.

72. The use of any one of claims 55-65, wherein about 9.0 g of the mixed salt oxybate is to be administered per day.

73. The use of claim 72, wherein about 4.5 g of the mixed salt oxybate is to be administered twice per day.

74. The use of any one of claims 55-73, wherein the mixed salt oxybate composition is a liquid.

75. The use of claim 74, wherein the concentration of the mixed salt oxybate in the liquid is from 350 mg/ml-650 mg/ml, or about 450 mg/ml-550 mg/ml.

76. The use of claim 74, wherein the concentration of the mixed salt oxybate in the liquid is about 0.5 g/mL.

77. The use of any one of claims 55-75 wherein the patient is treated for cataplexy.

78. The use of any one of claims 55-75, wherein the patient is treated for excessive daytime sleepiness in patients with narcolepsy.

79. The use of any one of claims 55-78, wherein the mixed salt oxybate is to be administered at bedtime.

80. The use of any one of claims 55-79, wherein the mixed salt oxybate is to be administered at bedtime and about 2.5 h-4 h after the bedtime administration.

81. The use of any one of claims 1-27, wherein the amount of the sodium oxybate and the mixed salt oxybate are the same on a gram for gram basis.

82. The use of any one of claims 28-54, wherein the amount of sodium oxybate and mixed salt oxybate are the same on a gram for gram basis.