currently approved pharmaceutical treatments and/or dosages of agents that enable weight loss. Gastrointestinal adverse events have been reported to limit higher doses of agents having GLP1 receptor agonist activity. The US label for tirzepatide (May 2022) states that use of tirzepatide may be associated with gastrointestinal adverse reaction, sometimes severe. There is a need for a dosing regimen to enable administration of higher tirzepatide doses with acceptable patient experience. There is an important medical need for pharmaceutical agents to enable additional weight management, while preserving an overall acceptable risk/benefit profile and patient tolerability.

There is a need for pharmaceutical compositions with higher doses of tirzepatide that are stable for storage for at least 6 months.

Peptides have unique physiochemical properties that often present challenges for achieving stable, pharmaceutically elegant compositions. For example, self-association, aggregation, adsorption to surfaces, solubility, and chemical stability of peptides present unique challenges for enabling the desired peptide composition. Bak, et.al., "Physicochemical and Formulation Developability Assessment for Therapeutic Peptide Delivery—A Primer - PMC (nih.gov)" AAPS J. 2015 Jan; 17(1): 144–155.

The compositions, doses, and methods provide these benefits while maintaining an acceptable profile of safety risks and adverse events.

Summary

In an aspect, there is provided a pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; NaCl; and sodium phosphate; wherein the tirzepatide, or pharmaceutically acceptable salt concentration is from about 40 mg/mL to about 60 mg/mL.

In another aspect, there is provided a pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; NaCl; and dibasic sodium phosphate; wherein the tirzepatide concentration is selected from the group consisting of about 2.5 mg/mL, about 40 mg/mL, about 50 mg/mL, and about 60 mg/mL.

In another aspect, there is provided a pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the tirzepatide concentration is from about 40 mg/mL to about 60 mg/mL; wherein the pH of the composition is from about 6.7 to about 7.3.

In another aspect, there is provided a pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the tirzepatide concentration is selected from the group consisting of about 2.5 mg/mL, about 40 mg/mL, and about 50 mg/mL; wherein the pH of the composition is from about 6.7 to about 7.3.

In another aspect, there is provided a pharmaceutical composition as disclosed herein for use in the treatment of T2D.

In another aspect, there is provided a pharmaceutical composition as disclosed herein for use in the treatment of obesity.

In another aspect, there is provided use of a pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating diabetes.

In another aspect, there is provided use of a pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating obesity.

In another aspect, there is provided use of a pharmaceutical composition as disclosed herein in the manufacture of a medicament for the treatment of T2D.

In another aspect, there is provided a pharmaceutical composition as disclosed herein for use in therapy.

In another aspect, there is provided use of a tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management; wherein the subject has obesity, and wherein:

a subject with obesity and in need of additional weight management is identified;

a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is at least 15 mg, is to be administered to said subject for a minimum of four weeks; and

after administration of the at least 15 mg once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, for at least four weeks, a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is 5 mg greater than the last dose is to be administered; wherein the maximum once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, dose is 25 mg.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management, wherein:

a subject in need of additional weight management is identified;

15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject; and

after at least one week, 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 2 weeks; and

after administration of 20 mg tirzepatide, or a pharmaceutically acceptable salt thereof, once weekly for at least 2 weeks;

25 mg tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered once weekly.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management, wherein:

a subject in need of additional weight management is identified;

20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 2 weeks; and

after administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, for at least 2 weeks;

25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need thereof, wherein the tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered as a once weekly subcutaneous dose selected from the group consisting of 20 mg and 25 mg tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a pediatric patient in need of chronic weight management, wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be

administered for at least four weeks.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject with an initial body mass index (BMI) that is less than or equal to 27 kg/m^2, wherein the subject has at least one weight-related comorbidity, and wherein a once weekly tirzepatide selected from the group consisting of 20 mg tirzepatide or a pharmaceutically acceptable salt thereof, and 25 mg tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a subject in need thereof, wherein the subject in need of treatment is pediatric, and wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject for a minimum of four weeks.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a subject in need thereof, wherein the subject in need of treatment is pediatric; and wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject for a minimum of four weeks.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional weight management in a subject in need thereof wherein the subject has a BMI > 27 kg/m2 and at least one weight-related comorbidity; and wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof, is to be increased to 5 mg;

the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;

if additional weight management is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;

the dose is to be increased in 5.0 mg increments after at least 4 weeks at the current dose; and

the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional weight management in a subject in need thereof wherein the subject has obesity; wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof, is to be increased to 5 mg;

the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;

if additional weight management is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;

the dose is to be increased in 5.0 mg increments after at least 4 weeks at the current dose; and

the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional glycemic control in a subject in need thereof, wherein the subject has type 2 diabetes; and wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof, is to be increased to 5 mg;

the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;

if additional glycemic control is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;

the dose is to be increased in 5.0 mg increments after at least 4 weeks at the current dose; and

the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a

pharmaceutically acceptable salt thereof.

Detailed Description

The present invention provides a pharmaceutically- acceptable composition of tirzepatide, or a pharmaceutically acceptable salt thereof; comprising; greater than 30 mg/mL tirzepatide or a pharmaceutically acceptable salt thereof, a tonicity agent, and sodium phosphate.

In an embodiment, is a composition of tirzepatide or a pharmaceutically acceptable salt thereof, comprising greater than 30 mg/mL tirzepatide, or a pharmaceutically acceptable salt thereof, a tonicity agent, and dibasic sodium phosphate.

In an embodiment, is a composition of tirzepatide or a pharmaceutically acceptable salt thereof, comprising greater than 30 mg/mL, and up to 60 mg/mL, tirzepatide, or a pharmaceutically acceptable salt thereof, a tonicity agent, and dibasic sodium phosphate.

In an embodiment, a tonicity agent is NaCl. In an embodiment, the NaCl concentration is from about 7 mg/mL to about 9 mg/mL. In an embodiment the NaCl concentration is from about 7.4 mg/mL to about 9.0 mg/mL. In an embodiment, the

WE CLAIM:

1. A pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; NaCl; and sodium phosphate; wherein the tirzepatide, or pharmaceutically acceptable salt concentration is from about 40 mg/mL to about 60 mg/mL.

2. A pharmaceutical composition as claimed by Claim 1 wherein sodium phosphate is dibasic sodium phosphate.

3. A pharmaceutical composition as claimed by any one of Claims 1 to 2 wherein the composition pH is from about 6.5 to about 7.5.

4. A pharmaceutical composition as claimed by any one of Claims 1 to 3 wherein the composition pH is from about 6.7 to about 7.3.

5. A pharmaceutical composition as claimed by any one of Claims 1 to 4 wherein tirzepatide, or a pharmaceutically acceptable salt thereof, concentration is from about 40 mg/mL to about 50 mg/mL.

6. A pharmaceutical composition as claimed by any one of Claims 1 to 5 wherein tirzepatide is a free base.

7. A pharmaceutical composition as claimed by any one of Claims 2 to 6 wherein the dibasic sodium phosphate concentration is from about 0.7 mg/mL to about 1.5 mg/mL.

8. A pharmaceutical composition as claimed by any one of Claims 2 to 7 wherein the dibasic sodium phosphate concentration is about 1.34 mg/mL.

9. A pharmaceutical composition as claimed by any one of Claims 1 to 8 wherein the NaCl concentration is from about 7 mg/mL to about 9 mg/mL.

10. A pharmaceutical composition as claimed by any one of Claims 1 to 9 wherein the NaCl concentration is from about 7.4 mg/mL to about 9.0 mg/mL.

11. A pharmaceutical composition as claimed by any one of Claims 1 to 10 wherein NaCl concentration is about 8.2 mg/mL.

12. A pharmaceutical composition as claimed by any one of Claims 1 to 11 wherein the composition has shelf life stability for at least about 6 months.

13. A pharmaceutical composition as claimed by any one of Claims 1 to 12 wherein the composition has shelf life stability for at least about 2 years.

14. A pharmaceutical composition as claimed by any one of Claims 1 to 11 wherein the composition has in-use stability for at least about 3 months.

15. A pharmaceutical composition as claimed by any one of Claims 1 to 11 wherein the composition has in-use stability for at least about 6 months.

16. A pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; NaCl; and dibasic sodium phosphate; wherein the tirzepatide concentration is selected from the group consisting of about 2.5 mg/mL, about 40 mg/mL, about 50 mg/mL, and about 60 mg/mL.

17. A pharmaceutical composition as claimed by Claim 16, wherein the composition has shelf life stability for at least about 3 months.

18. A pharmaceutical composition as claimed by any one of Claims 16 and 17 wherein the composition has shelf life stability for at least about 6 months years.

19. A pharmaceutical composition as claimed by any one of Claims 16 to 18 wherein the composition has shelf life stability for at least about 2 years.

20. A pharmaceutical composition as claimed by any one of Claims 16 to 19 wherein tirzepatide, or a pharmaceutically acceptable salt thereof, concentration is selected from the group consisting of about 2.5 mg/mL, about 40 mg/mL, and about 50 mg/mL.

21. A pharmaceutical composition as claimed by any one of Claims 16 to 20, wherein the tirzepatide, or a pharmaceutically acceptable salt thereof, concentration is about 40 mg/mL or about 50 mg/mL.

22. A pharmaceutical composition as claimed by any one of Claims 16 to 20, wherein the tirzepatide, or a pharmaceutically acceptable salt thereof, concentration is about 2.5 mg/mL.

23. A pharmaceutical composition as claimed by any one of Claims 16 to 22, wherein dibasic sodium phosphate concentration is from about 0.7 mg/mL to about 1.5 mg/mL.

24. A pharmaceutical composition as claimed by any one of Claims 16 to 23 wherein dibasic sodium phosphate concentration is about 1.34 mg/mL.

25. A pharmaceutical composition as claimed by any one of Claims 16 to 24 wherein the NaCl concentration is from about 7 mg/mL to about 9 mg/mL.

26. A pharmaceutical composition as claimed by any one of Claims 16 to 25 wherein the NaCl concentration is from about 7.4 mg/mL to about 9.0 mg/mL.

27. A pharmaceutical composition as claimed by any one of Claims 16 to 26 wherein the NaCl concentration is about 8.2 mg/mL.

28. A pharmaceutical composition as claimed by any one of Claims 16 to 22 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is selected from the group consisting of 2.5, 40, and 50 mg/mL; dibasic sodium phosphate concentration is from about 0.7 mg/mL to about 1.5 mg/mL; and NaCl concentration is from about 7 mg/mL to about 9 mg/mL.

29. A pharmaceutical composition as claimed by any one of Claims 16 to 22 or Claim 28 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is selected from the group consisting of 2.5 mg/mL, 40 mg/mL, and 50 mg/mL; dibasic sodium phosphate concentration is about 1.34 mg/mL; and NaCl concentration is about 8.2 mg/mL.

30. A pharmaceutical composition as claimed by any one of Claims 16 to Claim 29 wherein the composition is presented in an automatic injection apparatus.

31. A pharmaceutical composition as claimed by any one of Claims 16 to Claim 30 wherein the pH of the composition is from about 6.5 to about 7.5.

32. A pharmaceutical composition as claimed by any one of Claims 16 to Claim 31 wherein the pH is from about 6.7 to about 7.3.

33. A pharmaceutical composition as claimed by any one of Claims 16 to 32 further comprising one or more preservatives.

34. A pharmaceutical composition as claimed by any one of Claims 16 to Claim 33; wherein the composition further comprises a preservative selected from the group consisting of metacresol and phenol.

35. A pharmaceutical composition as claimed by any one of Claims 16 to Claim 22 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is selected from 2.5 mg/mL, 40mg/mL, and 50 mg/mL; dibasic sodium phosphate is from 0.7 mg/mL to about 1.5 mg/mL; and NaCl concentration is from 7 mg/mL

to 9 mg/mL.

36. A pharmaceutical composition as claimed by any one of Claims 19 to Claim 35 wherein tirzepatide is a free base.

37. A pharmaceutical composition as claimed by any one of Claims 19 to Claim 36 wherein the dose of the composition is about 0.5mL.

38. A pharmaceutical composition as claimed by any one of Claims 19 to Claim 37 wherein the composition is to be administered using an automatic injection apparatus.

39. A pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the tirzepatide concentration is from about 40 mg/mL to about 60 mg/mL; wherein the pH of the composition is from about 6.7 to about 7.3.

40. A pharmaceutical composition as claimed by Claim 39 wherein tirzepatide is a free base.

41. A pharmaceutical composition as claimed by any one of Claims 39 to Claim 40 wherein the tirzepatide concentration is from about 40 mg/mL to about 50 mg/mL.

42. A pharmaceutical composition as claimed by any one of Claims 39 to Claim 41 wherein the tirzepatide concentration is selected from the group consisting of about 40mg/mL and about 50mg/mL

43. A pharmaceutical composition as claimed by any one of Claims 39 to 42 wherein the tirzepatide concentration is selected from the group consisting of 40mg/mL and 50mg/mL

44. A pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the tirzepatide concentration is selected from the group consisting of about 2.5 mg/mL, about 40 mg/mL, and about 50 mg/mL; wherein the pH of the composition is from about 6.7 to about 7.3.

45. A pharmaceutical composition as claimed by any one of Claims 1 to 44 wherein tirzepatide consists of SEQ ID NO:1.

46. A pharmaceutical composition as claimed by any one of Claims 1 to Claim 45 for use in the treatment of T2D.

47. A pharmaceutical composition as claimed by any one of Claims 1 to Claim 45 for use in the treatment of obesity.

48. Use of a pharmaceutical composition as claimed by any one of Claims 1 to Claim

45 in the manufacture of a medicament for treating diabetes.

49. The use as claimed by Claim 48 wherein the pharmaceutical composition is to be administered as a once weekly dose.

50. Use of a pharmaceutical composition as claimed by any one of Claims 1 to Claim 45 in the manufacture of a medicament for treating obesity.

51. The use as claimed by Claim 50 wherein the pharmaceutical composition is to be administered using an automatic injection apparatus.

52. The use as claimed by Claim 50 or 51 wherein the pharmaceutical composition is to be administered as a once weekly dose.

53. Use of a pharmaceutical composition as claimed by any one of Claims 1 to Claim 45 in the manufacture of a medicament for the treatment of T2D.

54. A pharmaceutical composition as claimed by any one of Claims 1 to Claim 45 for use in therapy.

55. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management; wherein the subject has obesity, and wherein:

a subject with obesity and in need of additional weight management is identified;

a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is at least 15 mg, is to be administered to said subject for a minimum of four weeks; and

after administration of the at least 15 mg once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, for at least four weeks, a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is 5 mg greater than the last dose is to be administered; wherein the maximum once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, dose is 25 mg.

56. The use as claimed by Claim 55 wherein at least one of the once weekly doses of tirzepatide, or a pharmaceutically acceptable salt thereof, is 20 mg.

57. The use as claimed by Claim 55 or 56, wherein

a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is 20 mg is to be administered to said subject for a minimum of four weeks; and

after administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, for at least four weeks, a once weekly dose of tirzepatide, or a pharmaceutically acceptable salt thereof, that is 25 mg is to be administered.

58. The use as claimed by any one of Claims 55 to Claim 57 wherein tirzepatide is a free base.

59. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management, wherein:
a subject in need of additional weight management is identified;
15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject; and
after at least one week, 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 2 weeks; and
after administration of 20 mg tirzepatide, or a pharmaceutically acceptable salt thereof, once weekly for at least 2 weeks;
25 mg tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered once weekly.

60. The use as claimed by Claim 59 wherein 20 mg once weekly tirzepatide or a pharmaceutically acceptable salt thereof is to be administered for at least 4 weeks.

61. The use as claimed by Claim 59 or 60 wherein 15 mg once weekly tirzepatide is to be administered for at least 4 weeks.

62. The use as claimed by any one of Claims 59 to 61 wherein tirzepatide is a free base.

63. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need of additional weight management, wherein:
a subject in need of additional weight management is identified;
20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 2 weeks; and
after administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, for at least 2 weeks;

25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to said subject.

64. The use as claimed by Claim 63 wherein 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered without prior administration of a once weekly 17.5 mg tirzepatide dose.

65. The use as claimed by Claim 63 or Claim 64 wherein 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt, is to be administered without prior administration of a once weekly 22.5 mg tirzepatide dose.

66. The use as claimed by any one of Claims 63 to Claim 65 wherein once weekly 20 mg tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered for a least 4 weeks.

67. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject in need thereof, wherein the tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered as a once weekly subcutaneous dose selected from the group consisting of 20 mg and 25 mg tirzepatide, or a pharmaceutically acceptable salt thereof.

68. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a pediatric patient in need of chronic weight management, wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered for at least four weeks.

69. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for chronic weight management in a subject with an initial body mass index (BMI) that is less than or equal to 27 kg/m^2, wherein the subject has at least one weight-related comorbidity, and wherein a once weekly tirzepatide selected from the group consisting of 20 mg tirzepatide or a pharmaceutically acceptable salt thereof, and 25 mg tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered.

70. The use as claimed by Claim 69 wherein 20 mg tirzepatide or a pharmaceutically acceptable salt thereof is to be administered once weekly.

71. The use as claimed by Claim 69 or Claim 70 wherein 25 mg tirzepatide or a pharmaceutically acceptable salt thereof is to be administered once weekly.

72. The use as claimed by any one of Claims 69 to Claim 71 wherein the tirzepatide, or a pharmaceutically acceptable salt thereof is to be administered subcutaneously.

73. The use as claimed by any one of Claims 69 to Claim 72 wherein tirzepatide is a free base.

74. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a subject in need thereof, wherein the subject in need of treatment is pediatric, and wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject for a minimum of four weeks.

75. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a subject in need thereof, wherein the subject in need of treatment is pediatric; and wherein 1.25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject for a minimum of four weeks.

76. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional weight management in a subject in need thereof wherein the subject has a BMI $\geq$ 27 kg/m^2 and at least one weight-related comorbidity; and wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof, is to be increased to 5 mg;

the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;

if additional weight management is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;

the dose is to be increased in 5.0 mg increments after at least 4 weeks at the current dose; and

the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

77. The use as claimed by Claim 76 wherein the maximum dose required for weight management is 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

78. The use as claimed by Claim 76 or Claim 77 wherein administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to result in greater body weight reduction than administration of 15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

79. The use as claimed by any one of claims 76 to 78 wherein the maximum dose required for weight management is 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

80. The use as claimed by any one of Claims 76 to Claim 79 wherein administration of 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to result in greater body weight reduction than administration of 15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

81. The use as claimed by any one of Claims 76 to Claim 80 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose of tirzepatide, or pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional body weight reduction.

82. The use as claimed by any one of Claims 76 to 81 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose or tirzepatide or a pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional glycemic control in the subject.

83. The use as claimed by any one of Claims 76 to 82 wherein tirzepatide is a free base.

84. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional weight management in a subject in need thereof wherein the subject has obesity; wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof, is to be increased to 5 mg;

the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;

if additional weight management is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;

the dose is to be increased in 5.0 mg increments after at least 4 weeks at the

current dose; and

the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

85. The use as claimed by Claim 84 wherein the maximum dose required for weight management is 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

86. The use as claimed by Claim 84 or Claim 85 wherein administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to result in greater body weight reduction than administration of 15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

87. The use as claimed by any one of Claims 84 to 86 wherein the maximum dose required for chronic weight management is 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

88. The use as claimed by any one of Claims 84 to Claim 87 wherein administration of 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to result in greater body weight reduction than administration of 15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

89. The use as claimed by any one of Claims 84 to Claim 88 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose of tirzepatide, or pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional body weight reduction.

90. The use as claimed by any one of Claims 84 to 89 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose or tirzepatide or a pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional glycemic control in the subject.

91. The use as claimed by any one of Claims 84 to Claim 90 wherein tirzepatide is a free base.

92. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for additional glycemic control in a subject in need thereof, wherein the subject has type 2 diabetes; and wherein:

a 2.5 mg once weekly tirzepatide dose; or a pharmaceutically acceptable salt thereof, is to be administered to said subject for at least 4 weeks;

after 4 weeks, the once weekly tirzepatide dose, or a pharmaceutically

acceptable salt thereof, is to be increased to 5 mg;
the dose is to be increased in 2.5 mg increments after at least 4 weeks at the current dose;
if additional glycemic control is required after at least 4 weeks at a 15 mg once weekly tirzepatide dose, or a pharmaceutically acceptable salt thereof;
the dose is to be increased in 5.0 mg increments after at least 4 weeks at the current dose; and
the maximum dosage is 25 mg subcutaneous once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

93. The use as claimed by Claim 92 wherein the maximum dose required for additional glycemic control is 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

94. The use as claimed by Claim 92 or Claim 93 wherein administration of 20 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof, is to result in greater glycemic control than administration of 15 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

95. The use as claimed by any one of Claims 92 to Claim 94 wherein the maximum dose required for glycemic control is 25 mg once weekly tirzepatide, or a pharmaceutically acceptable salt thereof.

96. The use as claimed by any one of Claims 92 to Claim 95 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose of tirzepatide, or pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional body weight reduction in the subject.

97. The use as claimed by any one of Claims 92 to 96 wherein the administration of a 5.0 mg increment increase after 4 weeks at the current dose or tirzepatide or a pharmaceutically acceptable salt thereof, is to be repeated when there is a need for additional glycemic control in the subject.

98. The use as claimed by any one of Claims 92 to Claim 97 wherein tirzepatide is a free base.