GIP/GLP1 AGONIST COMPOSITIONS

The present invention is a pharmaceutical GIP/GLP1 co-agonist peptide composition for subcutaneous injection. The composition comprises tirzepatide, NaCl, and dibasic sodium phosphate. The composition provides commercially acceptable shelf-life stability, in-use stability, and is associated with acceptable patient injection site experience. An alternative composition comprises tirzepatide, propylene glycol, and dibasic sodium phosphate that also provides acceptable shelf-life stability.

Diabetes mellitus is a chronic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. In type 2 diabetes mellitus ("T2D"), the combined effects of impaired insulin secretion and insulin resistance are associated with elevated blood glucose levels. Tirzepatide is a GIP/GLP1 co-agonist peptide useful in the treatment of diabetes. Tirzepatide is useful in the treatment of obesity.

US9474780 generally describes compositions containing a GIP/GLP1 agonist, administered by parenteral routes. US9474780 describes and claims tirzepatide. There is a desire for compositions of tirzepatide providing acceptable stability and acceptable patient injection site experience.

Summary

In one aspect of the present disclosure, there is provided a pharmaceutical composition comprising tirzepatide, or a pharmaceutically acceptable salt thereof;

an agent selected from the group consisting of NaCl and propylene glycol; and

dibasic sodium phosphate.

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

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

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

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

Description

The present invention seeks to meet these needs by providing pharmaceutically-acceptable compositions of tirzepatide, or a pharmaceutically acceptable salt thereof; comprising an agent selected from the group consisting of NaCl and propylene glycol; and dibasic sodium phosphate.

In an embodiment, the agent is NaCl. In an embodiment, the NaCl concentration is from about 6.2 mg/mL to about 9.5 mg/mL. In an embodiment the NaCl concentration is from about 7.0 mg/mL to about 9.0 mg/mL. In an embodiment, the NaCl concentration is about 8.2 mg/mL.

In an embodiment, the agent is propylene glycol. In an embodiment, the propylene glycol concentration is from about 12.0 mg/mL to about 18.0 mg/mL. In an embodiment the propylene glycol concentration is from about 14.0 mg/mL to about 16.0 mg/mL. In an embodiment, the propylene glycol concentration is about 15.0 mg/mL.

In an embodiment, the dibasic sodium phosphate concentration is from about 0.67 mg/mL to about 2.68 mg/mL. In an embodiment, the dibasic sodium phosphate is about

WE CLAIM:

1. A pharmaceutical composition comprising

   tirzepatide, or a pharmaceutically acceptable salt thereof;

   an agent selected from the group consisting of NaCl and propylene glycol; and

   dibasic sodium phosphate.

2. The pharmaceutical composition as claimed by Claim 1, wherein

   the tirzepatide, or a pharmaceutically acceptable salt thereof,

   concentration is from about 5 to about 30 mg/mL.

3. The pharmaceutical composition as claimed by Claim 2

   wherein the dibasic sodium phosphate concentration is from about 1.0 mg/mL to about 3.0 mg/mL.

4. The pharmaceutical composition as claimed by Claim 3 wherein

   the dibasic sodium phosphate concentration is from about 0.67 mg/mL to about 2.68 mg/mL.

5. The pharmaceutical composition as claimed by Claim 4 wherein the

   dibasic sodium phosphate concentration is about 1.34 mg/mL.

6. The pharmaceutical composition as claimed by Claim 1 wherein the

   tirzepatide, or a pharmaceutically acceptable salt thereof,

   concentration is selected from the group consisting of 5, 10, 15, 20, 25, and

   30 mg/mL.

7. The pharmaceutical composition as claimed by Claim 6 wherein the

   tirzepatide, or pharmaceutically acceptable salt thereof, concentration is selected from the group consisting of 10, 20, and 30 mg/mL.

8. The pharmaceutical composition as claimed by Claim 7

   wherein the agent is NaCl.

9. The pharmaceutical composition as claimed by Claim 8 wherein

   the concentration of NaCl is from about 6.2 mg/mL to about 9.5 mg/mL.

10. The pharmaceutical composition as claimed by Claim 9 wherein the concentration of NaCl is from about 7.0 mg/mL to about 9.0 mg/mL.
11. The pharmaceutical composition as claimed by Claim 10 wherein the NaCl concentration is about 8.2 mg/mL.
12. The pharmaceutical composition as claimed by Claim 1 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate concentration is from about 0.67 mg/mL to about 2.68 mg/mL; and NaCl concentration is from about 6.2 mg/mL to about 9.5 mg/mL.
13. The pharmaceutical composition as claimed by Claim 12 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate concentration is about 1.34 mg/mL; and NaCl concentration is about 8.2 mg/mL.
14. The pharmaceutical composition as claimed by Claim 13 wherein the composition is presented in an automatic injection apparatus.
15. The pharmaceutical composition as claimed by Claim 1 wherein the agent is propylene glycol.
16. The pharmaceutical composition as claimed by Claim 15 wherein the concentration of propylene glycol is from about 12.0 mg/mL to about 18.0 mg/mL.
17. The pharmaceutical composition as claimed by Claim 16 wherein the concentration of propylene glycol is from about 14.0 mg/mL to about 16.0 mg/mL.
18. The pharmaceutical composition as claimed by Claim 17 wherein the concentration of propylene glycol is about 15.0 mg/mL.

19. The pharmaceutical composition as claimed by Claim 1 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate concentration is from about 0.67 mg/mL to about 2.68 mg/mL; and propylene glycol concentration is from about 14.0 mg/mL to about 16.0 mg/mL.
20. The pharmaceutical composition as claimed by Claim 19 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate concentration is about 1.34 mg/mL; and propylene glycol concentration is about 15.0 mg/mL.
21. The pharmaceutical composition as claimed by Claim 20 wherein the composition is presented in an automatic injection apparatus.
22. The pharmaceutical composition as claimed by Claim 21 wherein the pH of the composition is from about 6.5 to about 7.5.
23. The pharmaceutical composition as claimed by Claim 22 wherein the pH is from about 6.7 to about 7.3.
24. The pharmaceutical composition as claimed by Claim 23 further comprising one or more preservatives.
25. The pharmaceutical composition as claimed by Claim 24 wherein the composition further comprises a preservative selected from the group consisting of metacresol and phenol.
26. The pharmaceutical composition as claimed by Claim 25 wherein the preservative is metacresol.
27. Thep harmaceutical composition as claimed by Claim 26 wherein the metacresol concentration is from about 2.0 mg/mL to about 4.0 mg/mL.
28. The pharmaceutical composition as claimed by Claim 27 wherein the metacresol concentration is about 3.15 mg/mL.
29. The pharmaceutical composition as claimed by Claim 25 wherein the preservative is phenol.

30. The pharmaceutical composition as claimed by Claim 29 wherein the phenol concentration is from about 3.0 mg/mL to about 7.0 mg/mL.
31. The pharmaceutical composition as claimed by Claim 30 wherein the phenol concentration is about 5.0 mg/mL.
32. The pharmaceutical composition as claimed by Claim 1 wherein tirzepatide, or

    pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate is from about 0.67 to about 2.68 mg/mL; propylene glycol is from about 12.0 mg/mL to about 15.0 mg/mL; and further comprising from about 2.0 mg/mL to about 4.0 mg/mL metacresol.
33. The pharmaceutical composition as claimed by Claim 1 wherein tirzepatide, or pharmaceutically acceptable salt thereof, concentration is from about 5 mg/mL to about 30 mg/mL; dibasic sodium phosphate is from about 0.67 to about 2.68 mg/mL; propylene glycol is from about 12.0 mg/mL to about 18.0 mg/mL; and further comprising from about 3.0 mg/mL to about 7.0 mg/mL phenol.
34. The pharmaceutical composition as claimed by Claim 33 wherein the volume of the composition dose is about 0.5 mL.
35. The pharmaceutical composition as claimed by Claim 34 wherein the composition is to be administered using an automatic injection apparatus.
36. Use of a pharmaceutical composition as claimed by Claim 33 in the manufacture of a medicament for treating diabetes.
37. The use of Claim 36, wherein the dose is to be administered using an automatic injection apparatus.
38. The use of Claim 37, wherein the dose is to be administered once weekly.
39. Use of a pharmaceutical composition as claimed by Claim 33 in the manufacture of a medicament for treating obesity.
40. The use of Claim 39, wherein the dose is to be administered using an

automatic injection apparatus.

41. The use of Claim 40, wherein the dose is to be administered once weekly.
42. A pharmaceutical composition as claimed by Claim 33 for use in the treatment of diabetes.
43. A pharmaceutical composition as claimed by Claim 33 for use in the treatment of obesity.