maintain long-term weight reduction. Available treatments for obesity are particularly unsatisfactory for patients with severe obesity. Successful treatment of obesity is associated with alleviation or prevention of T2D. There is a need for alternative treatment options to induce therapeutic weight loss in patients in need of such treatment. Compounds having a ratio that is about 2.5:1 to about 10:1 GIP receptor agonist potency to GLP-1 receptor agonist potency are useful for significantly improving weight management, and can prevent the manifestation of T2D in formerly obese patients susceptible to T2D.

WO2016/111971 describes peptides stated to have GLP-1 and GIP activity. WO2013/164483 also discloses compounds stated to have GLP-1 and GIP activity. US9474780 generally describes compositions containing a GIP/GLP1 co-agonist, administered by parenteral routes, and generally discloses a wide dosage range up to about 30 mg per person per week. US9474780 discloses the use of GIP/GLP1 co-agonists for treating diabetes, obesity, and other conditions. US9474780 describes and claims tirzepatide.

Summary

In an aspect of the present disclosure, there is provided a use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:

a) a titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter

b) a maintenance dose of that GIP:GLP-1 Peptide is to be administered;

wherein the titration dose is about 50% of the maintenance dose.

In another aspect of the present disclosure, there is provided a use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:

a) a first titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein

cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter

b) a second titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

c) a third titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

d) a maintenance dose of that GIP:GLP-1 Peptide is to be administered;

wherein the first titration dose is about 25% of the maintenance dose, the second titration dose is about 50% of the maintenance dose and the third titration dose is about 75% of the maintenance dose.

In a further aspect of the present disclosure, there is provided a use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:

a) a first titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter

b) a second titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

c) a third titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

d) a fourth titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

e) a fifth titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

f) a maintenance dose of that GIP:GLP-1 Peptide;

wherein the first titration dose is about 17% of the maintenance dose, the second titration dose is about 33% of the maintenance dose, the third titration dose is about 50% of the maintenance dose, the fourth titration is about 66% of the maintenance dose and the fifth titration dose is about 83% of the maintenance dose.

In another aspect of the present disclosure, there is provided a composition comprising a GIP:GLP-1 Peptide having GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1; and a pharmaceutically acceptable excipient.

Description

The present invention provides novel dosing regimens of a GIP:GLP-1 Peptide for use in the aforementioned therapies (glycemic control/diabetes, obesity) that include one or more titration doses and a maintenance dose. More specifically, the present invention provides novel dosing regimens that include a titration dose and a maintenance dose wherein the titration dose is about 50% of the maintenance dose and is administered about once weekly for a minimum of about 2 weeks before administration of the maintenance dose. In another aspect, the dosing regimen comprises three titration doses: the first being about 25% of the maintenance dose, the second being about 50% of the maintenance dose and the third being about 75% of the maintenance dose, and a maintenance dose wherein each titration dose is administered about once weekly for a minimum of about 2 weeks before the administration of the next higher dose. In yet a third embodiment, the dosing regimen comprises five titration doses: the first being about 17% of the maintenance dose, the second being about 33% of the maintenance dose, the third being about 50% of the maintenance dose, the fourth being about 66% of the maintenance dose and the fifth being about 83% of the maintenance dose wherein each titration dose is administered about once weekly for a minimum of about 2 weeks before the administration of the next higher dose. Further embodiments are dosing regimens as above where each titration

WE CLAIM:

1. Use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:
    a) a titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter
    b) a maintenance dose of that GIP:GLP-1 Peptide is to be administered;
    wherein the titration dose is about 50% of the maintenance dose.

2. Use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:
    a) a first titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter
    b) a second titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter
    c) a third titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter
    d) a maintenance dose of that GIP:GLP-1 Peptide is to be administered;
    wherein the first titration dose is about 25% of the maintenance dose, the second titration dose is about 50% of the maintenance dose and the third titration dose is about 75% of the maintenance dose.

3. Use of a GIP:GLP-1 Peptide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein:
    a) a first titration dose of a GIP:GLP-1 Peptide having a GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using a casein

cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1 is to be administered for a minimum of about two weeks; and thereafter

b) a second titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

c) a third titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

d) a fourth titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

e) a fifth titration dose of that GIP:GLP-1 Peptide is to be administered for a minimum of about two weeks; and thereafter

f) a maintenance dose of that GIP:GLP-1 Peptide;

wherein the first titration dose is about 17% of the maintenance dose, the second titration dose is about 33% of the maintenance dose, the third titration dose is about 50% of the maintenance dose, the fourth titration is about 66% of the maintenance dose and the fifth titration dose is about 83% of the maintenance dose.

4. A composition comprising a GIP:GLP-1 Peptide having GIP:GLP-1 receptor agonist potency ratio as measured after a 60 minute incubation using casein cAMP assay normalized against GIP and GLP-1 that is about 2.5:1 to about 10:1; and a pharmaceutically acceptable excipient.

5. A composition as claimed by Claim 4 wherein the composition is to be administered at least two weeks as an escalation dose.

6. A composition as claimed by Claim 4 wherein the composition is to be administered at least four weeks as an escalation dose.

7. A composition as claimed by any one of Claims 4 to 6 wherein the composition is to be administered as a maintenance dose for at least two weeks.