In the context of the present invention, AVE0010 includes pharmaceutically acceptable salts thereof. The person skilled in the art knows pharmaceutically acceptable salts of AVE0010. A preferred pharmaceutically acceptable salt of AVE0010 employed in the present invention is acetate.

Summary

In one aspect, the present disclosure refers to the use of a pharmaceutical composition comprising desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof in the manufacture of a medicament for reducing postprandial plasma glucose concentration in a diabetes type 2 patient, wherein the diabetes type 2 patient to be treated has a 2 hours postprandial plasma glucose concentration of at least 14 mmol/L and a body mass index of at least 30 kg/m^2, wherein the patient to be treated does not receive an antidiabetic treatment.

A first example of the present disclosure is the use of desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of diabetes mellitus type 2.

The subject to be treated by the medicament of the present disclosure suffering from diabetes type 2 may be an obese subject. In the present disclosure, an obese subject may have a body mass index of at least 30 kg/m^2.

The subject to be treated by the medicament of the present disclosure may be an adult subject. The subject may have an age of at least 18 years of may have an age in the range of 18 to 80 years, or 40 to 80 years, or 50 to 60 years.
The subject to be treated by the medicament of the present disclosure preferably does not receive an antidiabetic treatment, for instance by insulin or/and related compounds.

The subject to be treated by the medicament of the present disclosure may suffer from diabetes mellitus type 2 for at least 1 year or at least 2 years. In particular, in

the subject to be treated, diabetes mellitus type 2 has been diagnosed at least 1 year or at least 2 years before onset of therapy by the medicament of the present disclosure.

The subject to be treated may have a HbA_{1c} value of at least about 8 % or at least about 7,5%. The subject may also have a HbA_{1c} value of about 7 to about 10 %. The example of the present disclosure demonstrates that treatment by AVE0010 results in a reduction of the HbA_{1c} value in diabetes type 2 patients (see Tables 9, 10).

The active agent of the present disclosure is preferably used for improving glucose tolerance in the treatment of a patient suffering from diabetes type 2. Improving glucose tolerance means that the postprandial plasma glucose concentration is reduced by the active agent of the present disclosure. Reduction means in particular that the plasma glucose concentration reaches normoglycemic values or at least approaches these values.

In the present disclosure, normoglycemic values are blood glucose concentrations of in particular 60 – 140 mg/dl (corresponding to 3,3 bis 7,8 mM/L). This range refers in particular to blood glucose concentrations under fasting conditions and postprandial conditions.

The subject to be treated may have a fasting plasma glucose concentration of at least 8 mmol/L, at least 8,5 mmol/L or at least 9 mmol/L. These plasma glucose concentrations exceed normoglycemic concentrations. The example of the present disclosure demonstrates that treatment by AVE0010 results in a reduction of the blood glucose concentration in diabetes type 2 patients (see Table 15).

The subject to be treated may have a 2 hours postprandial plasma glucose concentration of at least 10 mmol/L, at least 12 mmol/L, or at least 14 mmol/L. These plasma glucose concentrations exceed normoglycemic concentrations. The example of the present disclosure demonstrates that treatment by AVE0010 results in a

reduction of the 2 hours postprandial plasma glucose concentration in diabetes type 2 patients (see Table 11).

The subject to be treated may have a glucose excursion of at least 2 mmol/L, at least 3 mmol/L, at least 4 mmol/L or at least 5 mmol/L. In the present disclosure, the glucose excursion is in particular the difference of the 2 hours postprandial plasma glucose concentration and the plasma glucose concentration 30 minutes prior to a meal test. In the context of the present disclosure, a meal test is… The example of the present disclosure demonstrates that treatment by AVE0010 results in a reduction of the glucose excursion in diabetes type 2 patients (see Table 12). ‘‘Postprandial” is a term that is well known to a person skilled in the art of diabetology. The term “postprandial” describes in particular the phase after a meal or/and exposure to glucose under experimental conditions. In a healthy person this phase is characterised by an increase and subsequent decrease in blood glucose concentration. The term “postprandial” or “postprandial phase” typically ends up to 2h after a meal or/and exposure to glucose.

A second example of the present disclosure is the use of desPro^{36}Exendin-4(1-39)-Lys_6-NH_2 or/and a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for inducing weight loss in diabetes type 2 patients or/and for preventing weight gain in diabetes type 2 patients. The example of the present disclosure demonstrates that treatment by AVE0010 results in a weight reduction in diabetes type 2 patients (see Tables 13 and 14).

The active agent, the medicament or/and the pharmaceutical composition of the present disclosure can be used in the treatment of one or more of the medical indications described herein, for example in treatment of diabetes type 2 patients, or for conditions associated with diabetes type 2, such as reduction of the fasting plasma glucose concentration, reduction of the postprandial plasma glucose concentration, improvement of glucose tolerance, weight loss or/and prevention of weight gain.

In the present disclosure, desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ may be administered to a subject in need thereof, in an amount sufficient to induce a therapeutic effect.

The compound desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof may be administered parenterally, e.g. by injection (such as by intramuscular or by subcutaneous injection). Suitable injection devices, for instance the so-called "pens" comprising a cartridge comprising the active ingredient, and an injection needle, are known. The compound desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof may be administered in a suitable amount, for instance in an amount in the range of 10 to 15 µg per dose or 15 to 20 µg per dose.

In the present disclosure, desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof may be administered in a daily dose in the range of 10 to 20 µg, in the range of 10 to 15 µg, or in the range of 15 to 20 µg. DesPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof may be administered by one injection per day.

Yet another example of the present disclosure is a pharmaceutical composition comprising desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof, and optionally comprising pharmaceutically acceptable carriers, adjuvants, or/and auxiliary substances.

The pharmaceutical composition of the present disclosure may be prepared for use in the treatment of diabetes mellitus type 2.

The pharmaceutical composition of the present disclosure may also be prepared for use in inducing weight loss in diabetes type 2 patients or/and for use in preventing weight gain in diabetes type 2 patients.

The pharmaceutical composition of the present disclosure may also be prepared for use in the treatment of a subject as described herein.

In the present disclosure, the pharmaceutical composition or/and the medicament described herein may be a liquid composition comprising desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof. The skilled person knows liquid compositions of AVE0010 suitable for parenteral administration. A liquid composition of the present disclosure may have an acidic or a physiologic pH. An acidic pH preferably is in the range of pH 1 – 6.8, pH 3.5 - 6.8, or pH 3.5 – 5. A physiologic pH preferably is in the range of pH 2.5 - 8.5, pH 4.0 - 8.5, or pH 6.0 - 8.5. Preferably the range is of pH 4,5 – 5,0.
The pH may be adjusted by a pharmaceutically acceptable diluted acid (typically HCl) or pharmaceutically acceptable diluted base (typically NaOH).

The liquid composition of the present disclosure may comprise a suitable preservative. A suitable preservative may be selected from phenol, m-cresol, benzyl alcohol and p-hydroxybenzoic acid ester. A preferred preservative is m-cresol.

The liquid composition of the present disclosure may comprise a tonicity agent. A suitable tonicity agent may be selected from glycerol, lactose, sorbitol, mannitol, glucose, NaCl, calcium or magnesium containing compounds such as $CaCl_2$. The concentration of glycerol, lactose, sorbitol, mannitol and glucose may be in the range of 100 – 250 mM. The concentration of NaCl may be up to 150 mM. A preferred tonicity agent is glycerol.

The liquid composition of the present disclosure may comprise methionine.
Yet another example of the present disclosure is a method for the treatment of diabetes mellitus type 2 comprising administering desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof to a subject in need thereof.

A further example of the present disclosure is a method for inducing weight loss in diabetes type 2 patients or/and for preventing weight gain in diabetes type 2 patients, said method comprising administering desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof to a subject in need thereof.

In the method of the present disclosure, the subject may be the subject defined herein.

In the method of the present disclosure, the pharmaceutical composition or/and medicament as described herein may be administered.

The disclosure is further illustrated by the following example and figures.

Claims

1. Use of a pharmaceutical composition comprising desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and a pharmaceutically acceptable salt thereof in the manufacture of a medicament for reducing postprandial plasma glucose concentration in a diabetes type 2 patient, wherein the diabetes type 2 patient to be treated has a 2 hours postprandial plasma glucose concentration of at least 14 mmol/L and a body mass index of at least 30 kg/m^2, wherein the patient to be treated does not receive an antidiabetic treatment.

2. The use according to claim 1, wherein the patient to be treated is an adult subject.

3. The use of any of the preceding claims, wherein in the patient to be treated, diabetes mellitus type 2 has been diagnosed at least 1 year or at least 2 years before onset of therapy.

4. The use of any of the preceding claims, wherein the patient to be treated has a HbA$_{1c}$ value of 7 to 10%.

5. The use of any of the preceding claims, wherein the patient to be treated has a fasting plasma glucose concentration of at least 8 mmol/L.

6. The use of any of the preceding claims, wherein the desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and the pharmaceutically acceptable salt thereof is to be administered parenterally.

7. The use according to any of the preceding claims, wherein the pharmaceutical composition is prepared for administration of desPro^{36}Exendin-4(1-39)-Lys$_6$-NH$_2$ or/and the pharmaceutically acceptable salt thereof in a daily dose selected from the range of 10 µg

to 20 µg.

8. The use according to any of the preceding claims, wherein the pharmaceutical composition is prepared for once daily administration.

9. The use according to any of the preceding claims, wherein the pharmaceutical composition is further comprising pharmaceutically acceptable carriers, adjuvants, or/and auxiliary substances.