[Claims]

[Claim 1] Use of a pharmaceutical composition in the manufacture of a medicament for treating congenital hyperinsulinism, wherein the pharmaceutical composition comprises a peptide comprising the amino acid sequence of the following General Formula 1:

X1-X2-QGTF-X7-SD-X10-S-X12-X13-X14-X15-X16-X17-X18-X19-X20-X21-F-X23-X24-W-L-X27-X28-X29-X30 (General Formula 1, SEQ ID NO: 45)

wherein, in General Formula 1,
X1 is tyrosine (Y);
X2 is aminoisobutyric acid (Aib);
X7 is threonine (T), valine (V), or cysteine (C);
X10 is tyrosine (Y);
X12 is lysine (K);
X13 is tyrosine (Y) or cysteine (C);
X14 is leucine (L) or cysteine (C);
X15 is aspartic acid (D) or cysteine (C);
X16 is glutamic acid (E), serine (S), or cysteine (C);
X17 is lysine (K), arginine (R), –cysteine (C), or valine (V);
X18 is arginine (R), or cysteine (C);
X19 is alanine (A) or cysteine (C);
X20 is glutamine (Q), –or lysine (K);
X21 is aspartic acid (D), glutamic acid (E), or cysteine (C);
X23 is valine (V);
X24 is glutamine (Q);
X27 is methionine (M);
X28 is asparagine (N), or arginine (R);
X29 is threonine (T); and
X30 is cysteine (C) or is absent;
with the proviso that when the amino acid sequence of General Formula 1 is identical to SEQ ID NO: 1 or SEQ ID NO: 12, it is excluded,
wherein the peptide is a native glucagon derivative capable of activating a glucagon receptor.

[Claim 2]
Use of a pharmaceutical composition in the manufacture of a medicament for treating congenital hyperinsulinism, wherein the pharmaceutical composition comprises an isolated conjugate comprising a peptide moiety and a biocompatible material moiety which is linked to the peptide moiety, wherein the peptide moiety comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 14, 17, 19 to 25, 27, 29, 33, 35, 37, 38, 40 to 42 and 44-.

[Claim 3]

The use of claim 1,

wherein, in General Formula 1,

X1 is tyrosine (Y);

X2 is aminoisobutyric acid (Aib);

X7 is cysteine (C), threonine (T), or valine (V);

X10 is tyrosine (Y) ;

X12 is lysine (K) ;

X13 is tyrosine (Y) or cysteine (C);

X14 is leucine (L) or cysteine (C);

X15 is aspartic acid (D) or cysteine (C);

X16 is glutamic acid (E), serine (S), or cysteine (C);

X17 is , lysine (K), arginine (R), cysteine (C), or valine (V);

X18 is arginine (R) or cysteine (C);

X19 is alanine (A) or cysteine (C);

X20 is glutamine (Q) or lysine (K);

X21 is aspartic acid (D), glutamic acid (E), or cysteine (C);

X23 is valine (V);

X24 is glutamine (Q);

X27 is methionine (M);

X28 is asparagine (N) or arginine (R);

X29 is threonine (T); and

X30 is cysteine (C) or is absent.

[Claim 4]

The use of claim 1,

wherein, in General Formula 1,

X1 is tyrosine (Y);

X2 is aminoisobutyric acid (Aib);

X7 is cysteine (C), threonine (T), or valine (V);

X10 is tyrosine (Y) ;

X12 is lysine (K);

X13 is tyrosine (Y) or cysteine (C);

X14 is leucine (L) or cysteine (C);

X15 is aspartic acid (D) or cysteine (C);

X16 is glutamic acid (E), serine (S), or cysteine (C);

X17 is lysine (K), arginine (R), cysteine (C), or valine (V);

X18 is arginine (R) or cysteine (C);

X19 is alanine (A) or cysteine (C);

X20 is glutamine (Q) or lysine (K);

X21 is aspartic acid (D), glutamic acid (E), or cysteine (C);

X23 is valine (V);

~~X24 is glutamine (Q);~~
~~X27 is methionine (M);~~
~~X28 is asparagine (N) or arginine (R);~~
~~X29 is threonine (T); and~~
~~X30 is cysteine (C) or is absent.~~

[Claim 35~~5~~]
The use of claim 1,
wherein, in General Formula 1,
X1 is tyrosine (Y);
X2 is aminoisobutyric acid (Aib);
X7 is threonine (T), valine (V), or cysteine (C);
X10 is tyrosine (Y);
X12 is lysine (K);
X13 is tyrosine (Y) or cysteine (C);
X14 is leucine (L) or cysteine (C);
X15 is aspartic acid (D) or cysteine (C);
X16 is glutamic acid (E), serine (S), or cysteine (C);
X17 is lysine (K), arginine (R), ~~,~~ cysteine (C), or valine (V);
X18 is arginine (R), or cysteine (C);
X19 is alanine (A) or cysteine (C);
X20 is glutamine (Q), ~~,~~ or lysine (K);
X21 is aspartic acid (D) or glutamic acid (E);
X23 is valine (V);
X24 is ~~,~~ glutamine (Q);
X27 is ~~,~~ methionine (M);
X28 is asparagine (N) or arginine (R);
X29 is threonine (T); and
X30 is cysteine (C) or is absent.

[Claim 64~~6~~]
The use of claim 1,
wherein, in General Formula 1,
X1 is tyrosine (Y);
X2 is aminoisobutyric acid (Aib);
X7 is threonine (T);
X10 is tyrosine (Y);
X12 is lysine (K);
X13 is tyrosine (Y);
X14 is leucine (L);
X15 is aspartic acid (D) or cysteine (C);
X16 is glutamic acid (E), serine (S), or cysteine (C);
X17 is lysine (K) or arginine (R);

X18 is arginine (R);
X19 is alanine (A);
X20 is glutamine (Q), lysine (K);
X21 is aspartic acid (D), cysteine (C), or glutamic acid (E);
X23 is valine (V)-;
X24 is glutamine (Q) ;
X27 is methionine (M);
X28 is asparagine (N) or arginine (R);
X29 is threonine (T); and
X30 is absent.

[Claim 57]

The use of claim 1, wherein the peptide comprises the amino acid sequence of the following General Formula 2:

Y-Aib-QGTF-X7-SD-X10-S-X12-Y-L-X15-X16-X17-R-A-X20-X21-F-V-X24-W-L-M-N-T-X30 (General Formula 2, SEQ ID NO: 46)

wherein, in General Formula 2,
X7 is threonine (T), valine (V), or cysteine (C);
X10 is tyrosine (Y) or cysteine (C);
X12 is lysine (K) or cysteine (C);
X15 is aspartic acid (D) or cysteine (C);
X16 is glutamic acid (E) or serine (S);
X17 is lysine (K) or arginine (R);
X20 is glutamine (Q) or lysine (K);
X21 is aspartic acid (D) or glutamic acid (E);
X24 is glutamine (Q); and
X30 is cysteine (C) or is absent.

[Claim 86]

The use of claim 1, wherein the peptide has an isoelectric point (pI) value different from that of native glucagon (6.8).

[Claim 97]

The use of claim 1, wherein each amino acid in at least one amino acid pair among the amino acid pairs of X12 and X16, X16 and X20, X17 and X21 in General Formula 1 is substituted with glutamic acid or lysine, which is capable of forming a ring, respectively.

[Claim 108]

The use of claim 97, wherein each amino acid in the amino acid pair of X12 and X16 or each amino acid in the amino acid pair of X16 and X20 or each amino

acid in the amino acid pair of X17 and X21 is respectively substituted with glutamic acid or lysine, which is capable of forming a ring.

[Claim ~~11~~9]

The use of claim 1, wherein, in General Formula 1, a ring is formed between each amino acid in at least one amino acid pair among the amino acid pairs of X12 and X16, X16 and X20, X17 and X21.

[Claim ~~12~~10]

The use of claim 1, wherein the C-terminus of the peptide is amidated.

[Claim 11~~13~~]

The use of claim 1, wherein the C-terminus of the peptide is unmodified.

[Claim 12~~14~~]

The use of claim 5~~7~~, wherein the peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 37, 38, 40 to 42 and 44.

[Claim 13~~15~~]

The use of claim 1, wherein the peptide comprises the amino acid sequence of SEQ ID NO: 37.

[Claim 14~~16~~]

The use according to any one of claims 1,3,4,6 to 11 and 13~~ to 15~~, wherein the peptide is in the form of a long-acting conjugate, in which a biocompatible material moiety is linked to a peptide moiety comprising the amino acid sequence of General Formula 1.

[Claim ~~17~~15]

The use of claim 16, wherein the biocompatible material moiety is selected from the group consisting of a polymer, fatty acid, cholesterol, albumin and a fragment thereof, an albumin-binding material, a polymer of repeating units of a particular amino acid sequence, an antibody, an antibody fragment, an FcRn-binding material, *in vivo* connective tissue or a derivative thereof, a nucleotide, fibronectin, transferrin, a saccharide, heparin, and elastin.

[Claim ~~18~~16]

The use of claim ~~17~~15, wherein the polymer is selected from the group consisting of a polyethylene glycol, a polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer, a lipid polymer, chitin, hyaluronic acid, an oligonucleotide, and a combination thereof.

[Claim ~~19~~17]

The use of claim ~~17~~15, wherein the FcRn-binding material is a polypeptide comprising an immunoglobulin Fc region.

[Claim ~~20~~18]

The use of claim ~~16~~14, wherein the peptide moiety and the biocompatible material moiety are linked with each other through a linker.

[Claim ~~21~~19]

The use of claim ~~20~~18, wherein the linker is selected from the group consisting of a peptide, fatty acid, a saccharide, a polymer, a low molecular weight compound, a nucleotide, and a combination thereof.

[Claim 20~~22~~]

The use of claim 19~~21~~, wherein the polymer is selected from the group consisting of a polyethylene glycol, a polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer, a lipid polymer, chitin, hyaluronic acid, an oligonucleotide, and a combination thereof.

[Claim 21~~23~~]

The use of claim 22~~20~~, wherein the linker is a polyethylene glycol.

[Claim 22~~24~~]

The use of claim 17~~19~~, wherein the immunoglobulin Fc region is aglycosylated.

[Claim 23~~25~~]

The use of claim 17~~19~~, wherein the immunoglobulin Fc region is selected from the group consisting of:

(a) a CH1 domain, a CH2 domain, a CH3 domain, and a CH4 domain;

(b) a CH1 domain and a CH2 domain;

(c) a CH1 domain and a CH3 domain;

(d) a CH2 domain and a CH3 domain;

(e) a combination between one or at least two domains among a CH1 domain, a CH2 domain, a CH3 domain, and a CH4 domain, and an immunoglobulin hinge region or a part of the hinge region; and

(f) a dimer between each domain of the heavy chain constant region and the light chain constant region.

[Claim 24~~26~~]

The use of claim 17~~19~~, wherein the polypeptide comprising an immunoglobulin Fc region is in the form of a dimer.

[Claim 2527]

The use of claim 1719, wherein the immunoglobulin Fc region is a native Fc derivative in which the region capable of forming a disulfide bond is deleted, a native Fc derivative in which a part of the amino acid(s) in the N-terminus is removed, a native Fc derivative in which a methionine residue is added to the N-terminus, a native Fc derivative in which a complement-binding site is deleted, or a native Fc derivative in which an antibody dependent cell mediated cytotoxicity (ADCC) site is deleted.

[Claim 2628]

The use of claim 1719, wherein the immunoglobulin Fc region is derived from an immunoglobulin selected from the group consisting of IgG, IgA, IgD, IgE, and IgM.

[Claim 2729]

The use of claim 2628, wherein the immunoglobulin Fc region is an IgG4 Fc region.

[Claim 2830]

The use of claim 1719, wherein the immunoglobulin Fc region is an aglycosylated Fc region derived from human IgG4.

[Claim 2931]

The use of claim 1820, wherein the linker is linked to a cysteine residue of a peptide comprising the amino acid sequence of General Formula 1.

[Claim 3032]

The use of claim 1820, wherein the linker is respectively linked to the peptide moiety and the biocompatible material moiety through covalent bonds, which are respectively formed by reacting one end of the linker with an amine group or thiol group of the biocompatible material moiety and reacting the other end of the linker with an amine group or thiol group of the peptide moiety including the amino acid sequence of General Formula 1.

[Claim 3133]

The use according to any one of claims 1 to 3032, wherein the pharmaceutical composition is to be administered to a subject in need thereof for treating congenital hyperinsulinism.