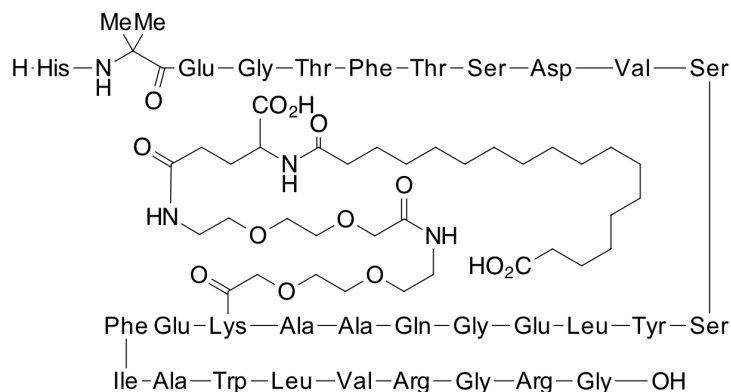


1. Monograph



Name: Semaglutide

Derivatives: 1 Semaglutide

Chemical name: N6,26-{18-[N-(17-carboxyheptadecanoyl)-L-gamma-glutamyl]-10-oxo-3,6,12,15-tetraoxa-9,18-diazaoctadecanoyl}-[8-(2-amino-2-propanoic acid),34-L-arginine]human glucagon-like peptide 1(7-37)

CAS: 910463-68-2

Mol formula: C₁₈₇H₂₉₁N₄₅O₅₉

Mol Wt: 4113.6

Originator: Novo Nordisk AS

Developer: Novo Nordisk

Uses: Antidiabetic , Anti-obesity

Market

Status: Launched

Patent Ref:

Acylated GLP-1 Compounds:

US2012295847 (2012) Priority : EP20050102171, 18 Mar. 2005 (Novo Nordisk AS, Denmark)

Acylated GLP-1 Compounds:

US2012295847 (2012) Priority : EP20050102171, 18 Mar. 2005 (Novo Nordisk AS, Denmark)

Preparation of XIX (21,39-di-tert-butyl 1-(2,5-dioxopyrrolidin-1-yl) 9,18,23-trioxo-2,5,11,14-tetraoxa-8,17,22-triazanonatriacontane-1,21,39-tricarboxylate) :

Semi-Recombinant Preparation Of GLP-1 Analogues:

US2010317057 (2010) Priority : EP20070124141, 28 Dec. 2007 (Novo Nordisk AS, Denmark)

Preparation of XX (18-tert-butoxy-18-oxooctadecanoic acid) :

Novel Insulin Derivatives:

US2006183668 (2006) Priority : DK20030001129, 05 Aug 2003 (Novo Nordisk AS, Denmark)

Preparation of XXI ((S)-4-amino-5-tert-butoxy-5-oxopentanoic acid) :

Process For Preparing Tert-butyl Ether Or Ester Containing Polyfunctional Organic Compounds:

US4485253 (1984) Priority : DE19813122450, 05 Jun. 1981 (Birr Christian, Germany)

Preparation of XXII (2-(2-(2-aminoethoxy)ethoxy)ethanoic acid)

Acylated GLP-1 Compounds:

US2012295847 (2012) Priority : EP20050102171, 18 Mar. 2005 (Novo Nordisk AS, Denmark)

Preparation of XXVI (octadecanedioic acid) :

Method For Producing Octadecanedioic Acid Through Synchronous Fermentation Of

Microorganisms:

CN102115769 (2011) Priority : CN20091256590, 30 Dec. 2009 (Wubo Cao, China)

Preparation of XXXVI (1-(9H-fluoren-9-yl)-3-oxo-2,7,10-trioxa-4-azadodecan-12-oic acid)

Methods Of Synthesizing And Using Derivatives Of [2-(2-aminoethoxy)ethoxy] Acetic Acid:

US2003134989 (2003) Priority : US20000253242P, 27 Nov. 2000 (University Of Maryland, US)

ACYLATED GLP-1 COMPOUNDS:

WO2006097537 (2006) Priority: EP20050102171, 18 Mar. 2005 (Novo Nordisk AS, Denmark)

DOUBLE-ACYLATED GLP-1 DERIVATIVES:

US2011166321 (2011) Priority: EP20090179390, 16 Dec. 2009 (Novo Nordisk AS, Denmark)

S.P. Marso et al., Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes., N Engl J Med. 2016 Sep 15.

M.A. Nauck et al., A Phase 2, Randomized, Dose-Finding Study of the Novel Once-Weekly Human GLP-1 Analog, Semaglutide, Compared With Placebo and Open-Label Liraglutide in Patients With Type 2 Diabetes, Diabetes Care. 2016 Feb;39(2):231-41.

J. Lau et al., Discovery of the Once-Weekly Glucagon-Like Peptide-1 (GLP-1) Analogue Semaglutide, J Med Chem. 2015 Sep 11.

C. Kapitza et al., Semaglutide, a once-weekly human GLP-1 analog, does not reduce the bioavailability of the combined oral contraceptive, ethinylestradiol/levonorgestrel, J Clin Pharmacol. 2015 May;55(5):497-504.

Technologies:

- solid phase peptide synthesis
- Enzymatic Oxidation
- Esterification
- Chromatographic separation
- Azide Synthesis

- Azide Reduction
- N-Protection
- OH-Oxidation
- N-Deprotection