

Retatrutide

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Retatrutide – a potent triple agonist (GLP-1/GIP/GCGR) for weekly administration. Clinical data show up to 24 % weight loss after 48 weeks and reduction of liver fat by over 82 %, placing Retatrutide among the most effective for obesity and metabolic disorders.

Product Features

Name: Retatrutide

Concentration: 10 mg

Form: Lyophilized (freeze-dried) powder

Purity: ≥ 99% (HPLC verified)

Receptor activity: GLP-1 / GIP / GCGR agonist

What Is Retatrutide?

Retatrutide (LY3437943) is an investigational triple hormone receptor agonist developed by Eli Lilly. It is the first compound designed to simultaneously activate three incretin and metabolic hormone receptors: GLP-1 (glucagon-like peptide-1), GIP (glucose-dependent insulintropic polypeptide), and glucagon.

Unlike the dual agonist Tirzepatide (GLP-1/GIP) or the mono-agonist Semaglutide (GLP-1), Retatrutide adds glucagon-receptor activation, which in studies is associated with additional increases in energy expenditure, lipolysis and reduced liver fat. In the literature, this combination of three mechanisms is described as the basis of a stronger metabolic effect than a single or dual agonist.

Retatrutide is being studied across several areas: obesity and overweight (TRIUMPH program), type 2 diabetes (TRANSCEND), metabolic dysfunction-associated steatotic liver disease (MASLD/NAFLD) and metabolic syndrome. According to publicly available data, the molecule remains an experimental candidate in Phase 3 clinical trials and holds no marketing authorization in any jurisdiction – it is not approved for clinical use. See also the other peptides for weight loss (GLP-1) in our category.

Key Characteristics:

Triple receptor agonist – simultaneously activates GLP-1, GIP, and glucagon receptors – the first compound to target all three

GLP-1 receptor – suppresses appetite, slows gastric emptying, enhances glucose-dependent insulin secretion

GIP receptor – improves insulin sensitivity, enhances lipid metabolism, and complements GLP-1 effects on insulin secretion

Glucagon receptor (novel) – increases energy expenditure, promotes hepatic fat oxidation, stimulates thermogenesis – the key differentiator from Semaglutide and Tirzepatide

Once-weekly injection – administered subcutaneously once per week with an estimated half-life of approximately 6 days

Investigational status – developed by Eli Lilly; currently in Phase 3 trials (TRIUMPH program). NOT FDA-approved. Approval not expected before late 2026–2027

Dosing & Titration Guide

Important: The information below describes schedules used in research on Retatrutide. It is provided for scientific and informational purposes and does not constitute a recommendation for individual use, medical advice or administration instructions. The research-grade Retatrutide offered by PurePepHub is not a registered medicine.

Unlike most research peptides, Retatrutide dosing is derived directly from a controlled clinical trial (Phase 2, Jastreboff et al., NEJM 2023) rather than animal-study extrapolation. The pivotal trial enrolled For research purposes only – not for human use. 338 adults with obesity or overweight, randomized to placebo or 1, 4, 8 or 12 mg weekly for 48 weeks, all using a titration schedule.

Maximum Weight Loss (12 mg/week)

The highest dose tested in the Phase 2 trial. Produced 24.2% mean weight loss at 48 weeks – the largest ever reported for an obesity pharmacotherapy. Requires the full 12-week titration protocol.

Target dose: 12 mg subcutaneously once weekly

Titration: 2 mg → 4 mg → 8 mg → 12 mg over 12 weeks

Duration: 48+ weeks (weight loss had not plateaued at 48 weeks in the trial)

GI side effects: Most common at this dose; nausea, diarrhea, and vomiting occur frequently during titration but generally improve

Moderate Weight Loss (8 mg/week)

Produced 22.8% mean weight loss – only 1.4 percentage points less than the 12 mg group but with somewhat fewer GI side effects. A strong option for those seeking efficacy with slightly better tolerability.

Target dose: 8 mg subcutaneously once weekly

Titration: 2 mg → 4 mg → 8 mg over 8 weeks

Duration: 48+ weeks

Notes: 100% of participants in this group lost at least 5% body weight; 93% lost at least 10%

Conservative Weight Loss (4 mg/week)

Even at 4 mg, Retatrutide produced 17.1% mean weight loss at 48 weeks – which exceeds the ~15% reported for Semaglutide 2.4 mg in the STEP 1 trial at 68 weeks. The lowest dose with meaningful triple agonist effect.

Target dose: 4 mg subcutaneously once weekly

Titration: 2 mg → 4 mg over 4 weeks

Duration: 48+ weeks

Notes: Fewest side effects of the effective dose groups; 93% achieved ≥5% weight loss

Retatrutide – storage and reconstitution

Retatrutide (Retagon) is supplied as a lyophilized powder in a vial. In lyophilized form the peptide is stable at room temperature, protected from light and moisture — refrigeration before reconstitution is not mandatory.

Before reconstitution: room temperature, in the original packaging, protected from light and moisture.

After reconstitution with bacteriostatic or sterile water: stability in the refrigerator +2 °C to +8 °C for up to 28 days. Do not refreeze the reconstituted solution.

Volume: max. 3 mL of solvent. For a precise calculation, use the peptide calculator.

Homogenization: add the solvent slowly down the vial wall, without vigorous shaking. Swirl gently, do not shake.

Worked example of reconstitution:

Vial size: 10 mg (10,000 mcg) of Retatrutide

Bacteriostatic water added: 2 mL

Concentration: $10 \text{ mg} \div 2 \text{ mL} = 5.0 \text{ mg per mL}$

Target dose: 4 mg

Volume to draw: $4 \div 5 = 0.8 \text{ mL} = 80 \text{ units on an insulin syringe}$

Injection Timing & Frequency

Frequency: Once weekly, on the same day each week

Time of day: Any time; morning or evening is fine. Consistency matters more than the specific time

Half-life: Approximately 6 days, supporting the once-weekly schedule

If switching injection days: Maintain at least 3 days between doses when transitioning to a new day of the week

Missed dose: If you miss your scheduled injection by 1–2 days, inject as soon as possible and resume your normal schedule. If more than 3 days late, skip the missed dose and resume on your next scheduled day.

Safety, Side Effects & Contraindications

Gastrointestinal Side Effects (Most Common)

GI side effects are dose-dependent — they are more frequent at higher doses and during the titration period. Most improve over time as the body acclimates.

Side Effect	Frequency (12 mg group)	Notes
Nausea	Up to 45%	Most common; peaks during titration, improves over time
Diarrhea	Up to 27%	More common at higher doses; usually mild to moderate
Vomiting	Up to 22%	More likely if titration is skipped or rushed; reduce dose if persistent
Constipation	Reported	Less common than nausea and diarrhea; increase fiber and water intake
Decreased appetite	Common	Expected pharmacological effect; ensure adequate nutrition despite reduced hunger

Glucagon Receptor-Specific Concerns

The glucagon receptor component distinguishes Retatrutide from other GLP-1-based treatments and introduces unique considerations:

Blood glucose monitoring: Glucagon promotes hepatic glucose production, which may partially counteract the glucose-lowering effects of GLP-1 and GIP. The net effect in the Phase 2 trial was improved glycemic control, but individual responses may vary. Regular blood glucose monitoring is strongly recommended, especially for diabetics and pre-diabetics.

Hepatic effects: Glucagon stimulates hepatic fat oxidation — a therapeutic benefit for fatty liver. However, baseline and periodic liver function tests (ALT, AST) are recommended to monitor hepatic effects.

Heart rate: GLP-1 agonists are associated with small increases in resting heart rate. The addition of glucagon receptor agonism could theoretically amplify this. Monitor resting heart rate, especially in the first weeks of treatment.

Expected Contraindications (Based on GLP-1 Agonist Class)

Because Retatrutide does not have an approved drug label, formal contraindications have not been established. However, based on the GLP-1 agonist class and the Phase 2 trial exclusion criteria, the following are expected contraindications:

- Personal or family history of medullary thyroid carcinoma (MTC) — GLP-1 agonists carry a class-wide boxed warning for thyroid C-cell tumors in rodent studies
- Multiple endocrine neoplasia syndrome type 2 (MEN2)
- History of pancreatitis — GLP-1 agonists have been associated with increased pancreatitis risk
- Pregnancy and breastfeeding — no safety data; avoid use entirely
- Type 1 diabetes — Retatrutide has not been studied in T1D; glucagon receptor agonism could worsen glycemic control
- Severe hepatic impairment — the glucagon component directly affects hepatic metabolism; use in liver disease has not been studied
- Severe renal impairment — insufficient data on use in advanced kidney disease

Recommended Baseline Labs

Before starting Retatrutide, obtain the following baseline bloodwork to enable ongoing monitoring:

- Fasting glucose and HbA1c
- Complete metabolic panel (CMP) including liver function (ALT, AST)
- Lipid panel (total cholesterol, LDL, HDL, triglycerides)
- Thyroid panel (TSH, free T4)
- Kidney function (BUN, creatinine, eGFR)
- Lipase and amylase (pancreatic markers)
- Resting heart rate and blood pressure