CLEAN PEPTIDES

Retatrutide Dosage Guide

Investigational triple agonist (GLP-1 / GIP / Glucagon) — titration schedules, reconstitution, injection technique and safety.

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What Is Retatrutide?

Investigational Drug Warning: Retatrutide (LY3437943) is NOT FDA-approved. It is an investigational compound currently in Phase 3 clinical trials. All dosing information in this guide is derived from a single Phase 2 trial and community protocols — not from an approved drug label. Using an unapproved investigational drug carries inherent risk.

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, GIP and glucagon. This triple mechanism distinguishes it from single agonists like Semaglutide (GLP-1 only) and dual agonists like Tirzepatide (GLP-1 + GIP).

The addition of glucagon receptor agonism is the novel element. While GLP-1 and GIP suppress appetite and enhance insulin secretion, glucagon increases energy expenditure, promotes hepatic fat oxidation and stimulates thermogenesis — mechanisms that drive additional weight loss. In the Phase 2 trial, Retatrutide at 12 mg per week produced 24.2% body weight loss at 48 weeks — the largest ever reported in an obesity drug trial.

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 and lipid metabolism.
- **Glucagon receptor (novel)** — increases energy expenditure, promotes hepatic fat oxidation and thermogenesis — the key differentiator.
- **Once-weekly injection** — administered subcutaneously with an estimated half-life of ~6 days.
- **Investigational status** — currently in Phase 3 trials (TRIUMPH program); approval not expected before late 2026–2027.

How Dosage Is Determined

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

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.

Phase 2 Results by Dose Group

Group	Mean Weight Loss	≥5% Loss	≥10% Loss	≥15% Loss
Placebo	-2.1%	27%	9%	5%
1 mg	-8.7%	64%	34%	19%
4 mg	-17.1%	93%	75%	57%
8 mg	-22.8%	100%	93%	83%
12 mg	-24.2%	100%	93%	83%

100% of participants in both the 8 mg and 12 mg groups lost at least 5% of body weight. The 12 mg group's 24.2% mean loss is the largest reported for any anti-obesity drug in a clinical trial.

Titration Schedule

Retatrutide requires gradual dose escalation over the first 12 weeks to minimize gastrointestinal side effects. All doses are once weekly, subcutaneous.

12 mg Target (Maximum Dose)

Period	Weekly Dose	Duration	Purpose
Step 1	2 mg	Weeks 1–4	Initial tolerance; GI acclimation
Step 2	4 mg	Weeks 5–8	First escalation; weight loss begins
Step 3	8 mg	Weeks 9–12	Second escalation; approaching therapeutic range
Maintenance	12 mg	Week 13+	Full therapeutic dose

8 mg Target

Period	Weekly Dose	Duration
Step 1	2 mg	Weeks 1–4
Step 2	4 mg	Weeks 5–8
Maintenance	8 mg	Week 9+

4 mg Target

Period	Weekly Dose	Duration
Step 1	2 mg	Weeks 1–4
Maintenance	4 mg	Week 5+

Community note: Some users start lower than the trial protocol — 0.5–1 mg for the first 1–2 weeks — to further reduce initial GI effects, extending each step by 1–2 weeks. **Do not skip titration.** Starting at the full target dose is the single most common mistake and leads to severe nausea, vomiting and diarrhea.

Retatrutide vs Semaglutide vs Tirzepatide

Feature	Retatrutide	Semaglutide	Tirzepatide
Receptors	GLP-1 + GIP + Glucagon	GLP-1 only	GLP-1 + GIP
FDA Status	Not approved (Phase 3)	Approved (Wegovy/Ozempic)	Approved (Zepbound/Mounjaro)
Max Dose	12 mg/week	2.4 mg/week	15 mg/week
Peak Weight Loss (trial)	24.2% at 48 wk	~15–17% at 68 wk	~22.5% at 72 wk
Half-life	~6 days	~7 days	~5 days
Titration Period	12 weeks	16–20 weeks	16–20 weeks

Cross-trial figures come from different populations and durations and are indicative, not head-to-head.

Reconstitution & Dosing (with the supplied 3 ml)

Clean Peptides also offers Retatrutide as a pre-filled click **pen** — see the separate Retatrutide Pen guide for a clicks-to-mg schedule.

Every Clean Peptides vial ships with **3 ml of bacteriostatic water** (0.9% benzyl alcohol). All figures below assume you reconstitute with the **full 3 ml**. On a standard U-100 insulin syringe, **100 units = 1 ml**.

Quick formula: concentration = vial strength ÷ 3 ml, and **units to draw = dose (mg) × 300 ÷ vial strength (mg)**.

How to reconstitute

1. **Wash your hands** and lay out the vial, the 3 ml bacteriostatic water, an insulin syringe and alcohol swabs on a clean surface.
2. **Flip off the caps** and swab both rubber stoppers with alcohol; let them air-dry 10–15 seconds.
3. **Draw the full 3 ml** of bacteriostatic water (in three 1 ml passes with an insulin syringe, or in one pass with a 3 ml syringe).
4. **Add the water slowly**, angling the needle so it runs down the inside glass wall — never squirt it directly onto the powder cake.
5. **Dissolve gently** — let the vial sit 1–2 minutes, then swirl or roll it between your palms until the solution is clear. Never shake.
6. **Label and refrigerate** at 2–8 °C. Resulting concentration: 15 mg → 5 mg/mL; 20 mg → 6.67 mg/mL; 30 mg → 10 mg/mL; 40 mg → 13.33 mg/mL.

Storage: unreconstituted powder refrigerated (2–8 °C); reconstituted solution refrigerated and used within 28–30 days; do not freeze; protect from light and heat.

Draw volumes with 3 ml — Retatrutide

Vial (Clean Peptides)	Concentration	2 mg	4 mg	8 mg	12 mg
15 mg	5 mg/mL	40 u	80 u	160 u*	240 u*
20 mg	6.67 mg/mL	30 u	60 u	120 u*	180 u*
30 mg	10 mg/mL	20 u	40 u	80 u	120 u*

Vial (Clean Peptides)	Concentration	2 mg	4 mg	8 mg	12 mg
40 mg	13.33 mg/mL	15 u	30 u	60 u	90 u

* This volume exceeds the 100-unit (1 mL) capacity of a standard insulin syringe — split it into two injections, or draw it with a 3 mL syringe.

Dosage by Goal

- **Maximum weight loss (12 mg/week):** 24.2% mean loss at 48 wk. Titrate 2→4→8→12 over 12 wk. GI effects most common at this dose.
- **Moderate weight loss (8 mg/week):** 22.8% mean loss with somewhat fewer GI effects. Titrate 2→4→8 over 8 wk.
- **Conservative (4 mg/week):** 17.1% mean loss — exceeds Semaglutide 2.4 mg. Fewest side effects of the effective groups.

The 8 mg and 12 mg groups produced similar results (22.8% vs 24.2%) but 12 mg had higher GI side-effect rates. Starting at 8 mg and evaluating for 8–12 weeks before escalating is a reasonable strategy.

Injection Guide

1. **Wash hands** and prepare a clean workspace.
2. **Swab the vial stopper**; air-dry 10–15 s.
3. **Draw your dose**; tap out air bubbles. For >100 units, split into two draws.
4. **Choose the site** — lower abdomen (2–3 in from navel), upper thigh, or back of upper arm. Rotate weekly.
5. **Clean the site** with alcohol; air-dry.
6. **Inject** into a pinched skin fold at 45°, plunger slow and steady.
7. **Dispose** in a sharps container; never recap or reuse.

Timing & frequency: once weekly, same day each week, any time of day. Half-life ~6 days. Missed dose ≤1–2 days late: inject ASAP and resume schedule; >3 days late: skip and resume next scheduled day. Rotate injection sites to prevent lipodystrophy.

Treatment Duration

Phase	Weeks	Description
Titration	Weeks 1–12	Gradual escalation from 2 mg; focus on GI tolerability
Active Weight Loss	Weeks 12–48	Full dose; most weight loss occurs here
Maintenance	Week 48+	Stabilization; discontinuation likely leads to regain

Based on Semaglutide and Tirzepatide data, discontinuing GLP-1-based treatments typically produces significant weight regain. Plan for long-term use if maintenance is the goal.

Stacking & Contraindicated Combinations

Do NOT combine with any other GLP-1 receptor agonist. Retatrutide already has full GLP-1 agonism built in; adding another creates redundant receptor activation with severely increased adverse-effect

risk.

Compound	Class	Why Not
Semaglutide	GLP-1 agonist	Redundant GLP-1 activation; severe GI, hypoglycemia risk
Liraglutide	GLP-1 agonist	Same mechanism overlap; only added risk
Tirzepatide	GLP-1/GIP dual agonist	Redundant on both receptors; dangerous overlap

No clinical stacking data exists for Retatrutide with any peptide or drug. The safest approach is standalone use.

Safety, Side Effects & Contraindications

Safety data is limited to a single Phase 2 trial (338 participants, 48 weeks). Long-term and rare adverse events are unknown.

Gastrointestinal (most common, dose-dependent)

Side Effect	Frequency (12 mg)	Notes
Nausea	Up to 45%	Peaks during titration, improves over time
Diarrhea	Up to 27%	Usually mild to moderate
Vomiting	Up to 22%	More likely if titration is skipped; reduce if persistent
Constipation	Reported	Increase fiber and water intake
Decreased appetite	Common	Expected effect; ensure adequate nutrition

Glucagon-Specific Concerns

- **Blood glucose monitoring** strongly recommended, especially for diabetics/pre-diabetics.
- **Hepatic effects** — baseline and periodic liver function tests (ALT, AST).
- **Heart rate** — monitor resting heart rate, especially early in treatment.

Expected Contraindications

Personal/family history of medullary thyroid carcinoma or MEN2; history of pancreatitis; pregnancy and breastfeeding; type 1 diabetes; severe hepatic or renal impairment.

Recommended Baseline Labs

Fasting glucose and HbA1c; complete metabolic panel with liver function; lipid panel; thyroid panel; kidney function; lipase and amylase; resting heart rate and blood pressure.

Common Mistakes

- Starting at full target dose without titrating.
- Treating Retatrutide dosing like Semaglutide (it is a triple agonist with glucagon activity).
- Combining with another GLP-1 agonist.
- Not monitoring blood glucose.

- Ignoring reconstitution math at high doses (12 mg at 10 mg/mL = 120 units, exceeding a 1 mL syringe).
- Not getting baseline labs before starting.

Key Takeaways

- First triple receptor agonist (GLP-1 + GIP + Glucagon); Phase 2 results up to 24.2% weight loss at 48 weeks.
- Titration is mandatory: 2 → 4 → 8 → 12 mg over 12 weeks.
- Once-weekly subcutaneous injection, ~6-day half-life.
- Do NOT combine with other GLP-1 agonists. Blood glucose monitoring and baseline labs are essential.
- NOT FDA-approved — Phase 3 (TRIUMPH); approval not expected before late 2026–2027. Available only via compounding/research suppliers.

References

1. Jastreboff AM, et al. "Triple-hormone-receptor agonist retatrutide for obesity — a Phase 2 trial." *N Engl J Med.* 2023;389(6):514-526.
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3. Nauck MA, et al. "GLP-1 receptor agonists in the treatment of type 2 diabetes — state-of-the-art." *Mol Metab.* 2021;46:101102.
4. Finan B, et al. "A rationally designed monomeric peptide triagonist corrects obesity and diabetes in rodents." *Nat Med.* 2015;21(1):27-36.
5. ClinicalTrials.gov. TRIUMPH 1 (NCT05929066); TRIUMPH 2 (NCT05929079).