

## RESEARCH DOSAGE MANUAL

# Retatrutide FlexPen

GLP-1R / GIPR / Glucagon Triple Agonist (LY3437943) · 30 mg / 3 ml · Research Grade

Triple incretin receptor agonist — Manufactured in the Netherlands under cGMP

INN / Code	Retatrutide (LY3437943)
CAS Number	2381704-71-6
Class	GLP-1R / GIPR / Glucagon Receptor Triple Agonist
Molecular Weight	~4,870 Da
Concentration	30 mg / 3 ml cartridge — 10 mg/ml
Pen Dose Scale	1 unit = 0.01 ml = 0.1 mg   10 units = 1 mg
Total Pen Doses	300 units per cartridge (30 mg total)
Purity	≥ 99.0% HPLC · Endotoxin < 1 EU/mg
Storage	2–8 °C · protect from light · do not freeze
Batch / Expiry	NL-2026-B · Expires 10/2029
Administration	Subcutaneous injection (research)

## 1. Compound Overview

Retatrutide (LY3437943) is the first unimolecular GLP-1R/GIPR/glucagon receptor triple agonist to enter clinical evaluation. Developed by Eli Lilly, it simultaneously activates three incretin and metabolic receptors to produce synergistic reductions in body weight and improvements in metabolic parameters. Phase 2 data published by Jastreboff et al. (NEJM, 2023) reported a mean body weight reduction of 24.2% at 12 mg/week over 48 weeks — the highest pharmacological weight-loss efficacy documented in a randomised controlled trial to that date.

Beyond adiposity, Retatrutide demonstrated reductions in hepatic fat (NASH models), improvements in insulin sensitivity, triglyceride lowering, and increased energy expenditure of approximately 15% through glucagon receptor-driven PPAR $\alpha$  activation and hepatic fatty acid beta-oxidation. It is an essential research tool for advanced metabolic, obesity, and cardiometabolic biology.

## 2. Mechanism of Action

- **GLP-1 receptor agonism:** Suppresses appetite via hypothalamic arcuate nucleus signalling, slows gastric emptying, and stimulates glucose-dependent insulin secretion.
- **GIP receptor agonism:** Enhances insulin sensitisation, promotes adipose tissue lipolysis, and exerts additive appetite suppression synergistic with GLP-1R.

- **Glucagon receptor agonism:** Drives hepatic glycogenolysis and fatty acid beta-oxidation via PPAR $\alpha$ , raises resting energy expenditure by ~15%, and promotes hepatic lipid clearance.
- **Synergistic triple action:** The combined receptor profile produces greater weight and metabolic outcomes than any single-receptor or dual-receptor agonist at equivalent doses.

### 3. FlexPen Operating Instructions

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The VitalPep Pro FlexPen is a reusable multi-dose injection pen pre-filled with Retatrutide (30 mg / 3 ml). Each unit on the dose dial delivers exactly 0.01 ml (10  $\mu$ l) of solution. The pen accepts standard 31-gauge or 32-gauge pen needles (4–8 mm). Follow the steps below before every injection.

#### ■ Step 1 — Prepare the pen

Remove the pen cap. Inspect the cartridge window: the solution should be clear and colourless. Do not use if particulates are visible or if the solution appears cloudy or discoloured. Attach a new sterile pen needle by screwing it clockwise until firmly seated. Remove both the outer and inner needle caps and set aside.

#### ■ Step 2 — Prime the needle

Select 2 units on the dose dial by turning the dial clockwise. Point the pen needle upward and tap the cartridge gently to collect any air bubbles at the top. Press the injection button fully until it clicks and a small stream (or droplet) appears at the needle tip. Repeat if no flow is seen. Priming removes air and confirms the pen is working correctly.

#### ■ Step 3 — Set your dose

Dial your required dose by turning the dose selector clockwise. For example, to inject 1 mg, dial to 10 units. The current dose is displayed in the dose window. You can turn anti-clockwise to reduce the dose before injecting — the pen will not dispense solution while dialling.

#### ■ Step 4 — Choose the injection site

Subcutaneous injection sites: abdomen (at least 5 cm from the navel), outer thigh, or upper arm. Rotate sites with each injection to avoid lipohypertrophy. Wipe the skin with an alcohol swab and allow to air-dry for 10 seconds before injecting.

#### ■ Step 5 — Inject

Pinch a fold of skin with two fingers. Insert the needle at a 45–90° angle (use 90° for a 4 mm needle, 45° for longer needles). Press the injection button slowly and firmly until it stops. Hold the button down and count to 10 seconds before withdrawing — this ensures full dose delivery and prevents backflow.

#### ■ Step 6 — Withdraw and recap

Withdraw the needle at the same angle it was inserted. Do not rub the injection site. Replace the outer needle cap using the one-hand scoop method, then unscrew and safely dispose of the used needle in a sharps container. Replace the pen cap. Never store the pen with the needle attached.

#### ■ Step 7 — Storage after use

Store the pen at 2–8 °C (refrigerated) when not in active use. Do not freeze. The pen may be kept at room temperature (up to 25 °C) for a maximum of 28 days during an active dosing cycle. Record the date of first use on the pen label.

■ Always use a new sterile needle for each injection. Sharing pens or needles poses a serious infection risk. The cartridge is pre-filled and sealed — do not attempt to refill or modify the pen.

## 4. Research Dosing Protocol

**Concentration** 10 mg/ml — 1 unit on the pen dial = 0.01 ml = 0.1 mg | 10 units = 1 mg | 120 units = 12 mg

Retatrutide is administered once weekly by subcutaneous injection. The Phase 2 escalation schedule below mirrors the Jastreboff et al. 2023 protocol and is the standard reference dosing framework on [peptidedosages.com](https://www.peptidedosages.com). Escalation allows GI tolerance to develop before reaching the active research dose.

### Weekly Dose Escalation Schedule

Phase	Weeks	Weekly Dose	Units to Dial	Volume (ml)	Frequency
Initiation	1–4	1 mg	10 units	0.10 ml	Once weekly
Escalation 1	5–8	2 mg	20 units	0.20 ml	Once weekly
Escalation 2	9–12	4 mg	40 units	0.40 ml	Once weekly
Escalation 3	13–16	8 mg	80 units	0.80 ml	Once weekly
Maintenance	17+	12 mg	120 units	1.20 ml	Once weekly

**Pen longevity:** At 12 mg/week maintenance (120 units), the 30 mg cartridge provides approximately 2.5 weekly doses. At the 4 mg/week escalation phase (40 units), the cartridge provides approximately 7.5 weekly doses.

**Dose day:** Choose a consistent weekly injection day. Administer on the same day each week. If a dose is missed by more than 2 days, skip and resume on the next scheduled day.

■ Retatrutide causes dose-dependent nausea in research models. Do not exceed the escalation schedule. If GI effects occur at a given dose level, remain at that dose for an additional 2 weeks before escalating. Never exceed 12 mg per weekly injection (120 units).

■ Monitor for hypoglycaemia when used alongside other metabolic research agents. Glucagon receptor agonism can suppress counter-regulatory glucose responses.

## 5. Storage & Handling

<b>In-use storage</b>	Up to 25 °C for a maximum of 28 days during active dosing cycle
<b>Between-use</b>	2–8 °C (refrigerated) · do not freeze
<b>Light protection</b>	Keep pen cap on at all times when not injecting
<b>Inspection</b>	Solution must be clear, colourless, and free of particles
<b>Expiry</b>	Do not use after printed expiry or 28 days post first puncture

## 6. Key References

Jastreboff AM et al. (2023). Triple-Hormone-Receptor Agonist Retatrutide for Obesity. *N Engl J Med.* 389(6):514–526.  
Coskun T et al. (2022). LY3437943, a novel triple GIP, GLP-1, and glucagon receptor agonist. *Mol Metab.* 66:101610.

Thomas MK et al. (2021). Characterisation of LY3437943 receptor binding and signalling profile. *J Pharmacol Exp Ther.* 379(3):345–357.  
peptidedosages.com — Retatrutide average research dosing protocols (accessed 2026).