

Retatrutide Patient Information

Introduction

Managing weight is a crucial aspect of overall health. Being overweight or obese is not just about appearance; it's a medical condition that significantly increases the risk of chronic diseases. This information sheet provides an overview of three medications—Tirzepatide, Semaglutide, and Retatrutide—designed to aid in weight loss and improve related health conditions.

Health Risks of Overweight and Obesity

Understanding the health risks associated with excess weight underscores the importance of weight management.

Cardiovascular Diseases

- Individuals with obesity have a **32% higher risk** of developing coronary artery disease compared to those with normal weight.
- Approximately **75%** of hypertension cases are related to obesity.

Type 2 Diabetes

- Around **90%** of individuals with type 2 diabetes are overweight or obese.
- Each **1-point** increase in Body Mass Index (BMI) is associated with a **7% increase** in the risk of developing diabetes.

Cancer Risk:

- Obesity is linked to an increased risk of at least **13 types** of cancer, including breast (post-menopause), colorectal, endometrial, kidney, liver, and pancreatic cancers.
- In the United States, about **40%** of all cancers diagnosed are now associated with overweight and obesity.

Sleep Apnea

- An estimated **70%** of individuals with obstructive sleep apnea are obese.
- Weight gain of **10%** can increase the risk of developing sleep apnea by six times.

Osteoarthritis

- For every **5 point** increase in BMI, the risk of osteoarthritis increases by **35%**.

Non-Alcoholic Fatty Liver Disease (NAFLD)

- Among obese individuals, the prevalence of NAFLD can be as high as **90%**.

Reproductive Health

- **Women:** Obesity can cause menstrual irregularities and infertility. Approximately **30%** of cases of infertility are related to weight issues.
- **Men:** Obesity is associated with lower testosterone levels, affecting fertility and sexual function.

Mental Health

- Individuals with obesity have a **55% increased risk** of developing depression over time. There is a bidirectional relationship; those with depression have a **58% increased risk** of becoming obese.

Mortality and Life Expectancy

- Each **5-point** increase in BMI above 25 is associated with a **31% higher risk** of premature death.
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Weight Loss Medications

Semaglutide, tirzepatide, and retatrutide belong to a class of diabetes and weight loss medications commonly referred to as GLP-1 (Glucagon-like Peptide) agonists. All of these medications affect GLP-1. However, tirzepatide also affects GIP (Glucose-dependent Insulinotropic Polypeptide), and retatrutide affects GLP-1, GIP, and Glucagon.

Receptors

- **GLP-1 (Glucagon-like peptide-1):** It enhances the release of insulin, which helps lower blood sugar levels, and slows down gastric emptying, which contributes to a feeling of fullness.
- **GIP (Glucose-dependent insulinotropic polypeptide):** This receptor helps enhance insulin secretion in response to meals, further supporting glucose regulation. It also contributes to metabolic processes that promote weight loss.
- **Glucagon receptors:** These are involved in regulating energy expenditure and promoting lipolysis (the breakdown of fats). Activation of glucagon receptors can increase metabolic rate, which may aid in weight reduction.

Remember that overweight and obesity are chronic medical conditions and frequently require chronic medication use. Contrary to popular belief, it's NOT just about eating less and exercising more. Many times, your body causes you to store fat easier, to not burn fat for energy, mistakenly tells you that you are hungry when you're not, and fights your attempts at losing weight. It is not "cheating" to use medication to control your weight any more than it is "cheating" to use blood pressure medication to control your blood pressure. Yes, your weight may increase if you stop the medication, the same way your blood pressure increases if you stop your blood pressure medication.

You absolutely have to have good eating habits and monitor calorie intake, make sure you are being active, and get enough sleep. It is also imperative that you consume an adequate amount of protein. You not only require protein to maintain your muscle mass, but all of your vital organs require a significant amount of protein. Try to consume about 1 gram of protein for every pound of body weight. For this, you use your GOAL body weight, not your current body weight. For example, if you currently weigh 200 lbs, but your goal/healthy weight is 140; you will aim for a daily intake of 140 grams. If you have any kidney dysfunction, please consult your nephrologist or primary care provider for daily protein recommendations. You have to track your protein intake. Most people significantly overestimate how much protein they consume. All of these things will increase your success with weight loss and help you keep the weight off!

I recommend taking these medications for at least 6 months. Your body wants to stay at the weight it is. You have a “set point” for a weight that your body will try to maintain. It takes a long time to lower that set point. If you want to keep the weight you have lost off, you have a better chance if you take the medication for 6 months or longer. You also have to make lifestyle and diet changes while you are taking the medication.

Retatrutide

What is Retatrutide?

Retatrutide (Pronounced Ret-uh-true-tide) is a once-weekly injectable investigational medication currently being studied for the treatment of obesity and type 2 diabetes. It is a novel peptide that functions as a triple hormone receptor agonist, targeting the receptors for glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), and glucagon. By activating all three receptors, retatrutide aims to provide enhanced metabolic benefits compared to medications that target only one or two of these pathways.

How Does Retatrutide Work?

GLP-1 Receptor Activation:

- **Increased Insulin Secretion:** Retatrutide stimulates the pancreas to release insulin in response to elevated blood glucose levels, aiding in blood sugar regulation.
- **Decreased Glucagon Secretion:** It suppresses the release of glucagon, a hormone that raises blood sugar levels, thereby contributing to better glycemic control.
- **Appetite Suppression:** Activation of GLP-1 receptors in the brain leads to reduced appetite and increased feelings of fullness, promoting weight loss.
- **Slowed Gastric Emptying:** It delays the rate at which food leaves the stomach, helping to prevent rapid spikes in blood sugar after meals.

GIP Receptor Activation:

- **Enhanced Insulin Release:** GIP works synergistically with GLP-1 to stimulate insulin secretion from the pancreas in a glucose-dependent manner.

- **Improved Insulin Sensitivity:** It may enhance the body's responsiveness to insulin, facilitating better glucose uptake by tissues.

Glucagon Receptor Activation:

- **Increased Energy Expenditure:** Activation of glucagon receptors promotes the breakdown of stored fats (lipolysis) and stimulates thermogenesis (heat production), leading to increased calorie burning.
 - **Weight Loss:** By enhancing fat breakdown and energy expenditure, retatrutide contributes to significant weight reduction beyond appetite suppression alone.
 - **Liver Effects:** While glucagon can stimulate glucose production in the liver, the balanced activation in retatrutide aims to mitigate adverse effects on blood sugar levels.
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Potential Health Benefits

- **Significant Weight Loss:** Clinical trials have shown that retatrutide can lead to substantial weight reduction. Participants experienced an average weight loss of 24% over 48 weeks, surpassing the results of existing weight-loss medications.
 - **Improved Glycemic Control:** Retatrutide has been effective in lowering blood sugar levels, making it a promising treatment for individuals with type 2 diabetes. In studies, participants achieved reductions in HbA1c levels, indicating better blood glucose management.
 - **Enhanced Cardiovascular Health:** The medication has been associated with improvements in cardiovascular risk factors, including reductions in blood pressure and lipid levels. These changes contribute to a decreased risk of heart disease.
 - **Reduction in Liver Fat:** Retatrutide has shown potential in reducing liver fat content, which is beneficial for individuals with non-alcoholic fatty liver disease (NAFLD). This effect may help mitigate the progression of liver-related conditions.
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Potential Side Effects

- **Gastrointestinal Issues:** These are common and can include nausea, vomiting, diarrhea, and constipation. These symptoms often occur at the beginning of treatment and may lessen over time.
- **Decreased Appetite:** While this can be a beneficial effect for weight loss, it may lead to reduced food intake that some individuals may find difficult to manage.
- **Potential Hypoglycemia:** Especially when used with other glucose-lowering medications, there may be a risk of low blood sugar levels.

- **Injection Site Reactions:** Some participants in trials reported mild to moderate reactions at the injection site, such as redness or irritation.
- **Dizziness and Headaches:** These were noted in some trial participants, usually occurring when the body adjusts to the medication.
- **Potential Gallbladder Issues:** As with other weight-loss drugs, significant weight loss can increase the risk of gallstones and other gallbladder-related problems.
- **Elevated Heart Rate:** Some participants have reported an increase in heart rate, which may need monitoring, especially in those with pre-existing heart conditions.
- **Skin Effects:** Significant weight loss may cause sagging skin and more pronounced wrinkles. This is not specific to GLP-1 medications. ANYTHING that causes significant weight loss will cause more pronounced wrinkles and sagging skin because the underlying supporting structure of your skin has been stretched out from being overweight. The more overweight you are, the more pronounced this effect is when you lose weight.
- If you develop intolerable nausea or vomiting, go back to the previous dose for a few more weeks and try to increase it again later. You do not have to increase to the maximum dose. If you are losing weight and not having significant side effects, you can maintain at that dose. If you develop severe constipation or abdominal pain, stop the medication and get evaluated by your PCP or Emergency Dept ASAP. If you develop swelling in your neck or difficulty swallowing, get evaluated by your PCP or Emergency Dept.

Dosage Guidelines

See Dosing Schedule at the end of this document.

Retatrutide is given as a weekly subcutaneous injection. The starting dose is 1mg weekly, and the maximum dose is 8mg weekly. Very few patients require the maximum dosage. The optimal dosage is one in which you are losing weight and don't have intolerable side effects. This is different for each patient.

If you experience intolerable side effects, like nausea and vomiting, go back to the dose you were at before for a week or two and try increasing it again. If intolerable nausea or vomiting persists, just stay at the dose you tolerate.

Cost

Retatrutide is an investigational drug in Phase 2 clinical trials at Lilly. It is currently only available as a research peptide. Please see document titled "Research Peptide Information" in the Education Folder under Records in the patient portal.

18mg Vial (1.8ml) (10mg/ml) - \$338.50 (Includes shipping and bacteriostatic water for reconstitution)

- **If you are just beginning treatment:** The first vial will last approximately 8 weeks.
- **Dosage of 4mg per week:** The vial will last approximately 4.5 weeks.
- **Dosage of 8mg per week:** The vial will last approximately 2.25 weeks.

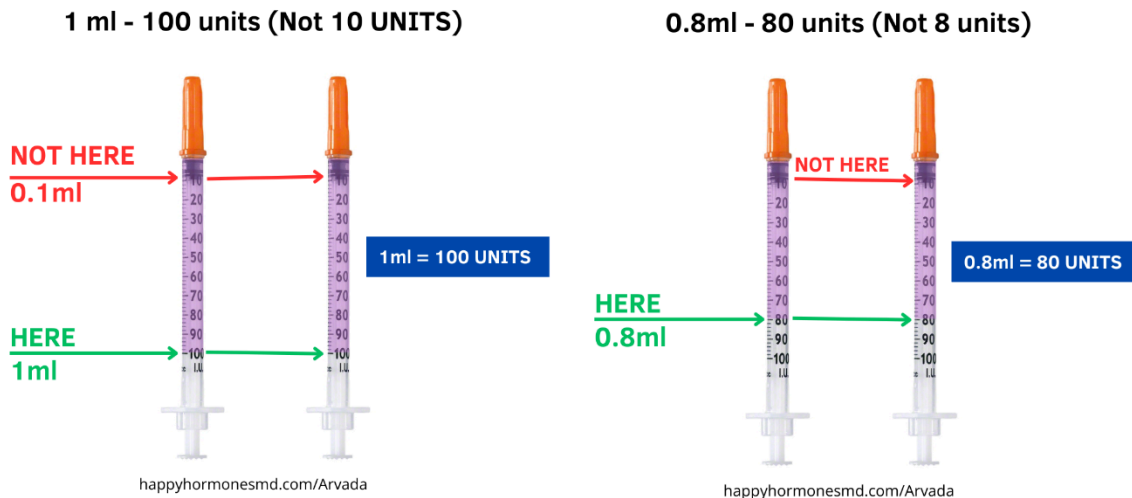
Reconstitution Instructions

IMPORTANT:

- Follow the instructions below regarding the amount of bacteriostatic water to use when reconstituting the peptide. **DO NOT** follow the instructions that come with the peptide.
- **Do NOT** throw away the vial of bacteriostatic water!!! It is a multiuse vial and can be used for your next order!

18mg Vial

Inject **1.8 ml** of bacteriostatic water into the vial of powder (1.8ml = 180 units).



- See the **document** titled “*Reconstituting Medications in Powder Form*” in the Education Folder in the patient portal.
- See the following **Instructional videos** in the Education Folder in the patient portal:
 - “*Reconstituting Powdered Medications*”

- *“Injection Video – Introduction”*
 - *“Injection Video – Drawing Up the Medication”*
 - *“Injection Video – Administering the Medication”*
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Storage and Stability for Research Peptides

- Vials are shipped as **lyophilized powder**, requiring no refrigeration during shipping.
 - In Lyophilized Form:
 - Stable for up to 3 years in the freezer and 2 years in the refrigerator.
 - Protect from light.
 - Once Reconstituted:
 - Stable for 6 weeks.
 - Must be refrigerated and kept away from light.
 - Avoid placing vials in the refrigerator door to prevent degradation from frequent temperature changes.
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Important Disclosures

- These statements have not been evaluated by the US Food and Drug Administration (FDA).
 - Not intended to diagnose, treat, cure, or prevent any disease.
 - Research peptides and some compounded drugs are not FDA-approved but are produced under strict quality control measures.
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Quality Assurance

- All research peptides are subjected to third-party testing with publicly available Certificates of Analysis (COA).
- Testing includes:
 - RP-HPLC (Reversed-Phase High-Performance Liquid Chromatography)
 - Mass Spectrometry (MS)
 - Sterility Testing

- Additional tests meeting or exceeding U.S. Pharmacopeia (USP) and USP-National Formulary (NF) regulations.

The manufacturer ensures quality, safety, and efficacy, complying with regulatory standards.

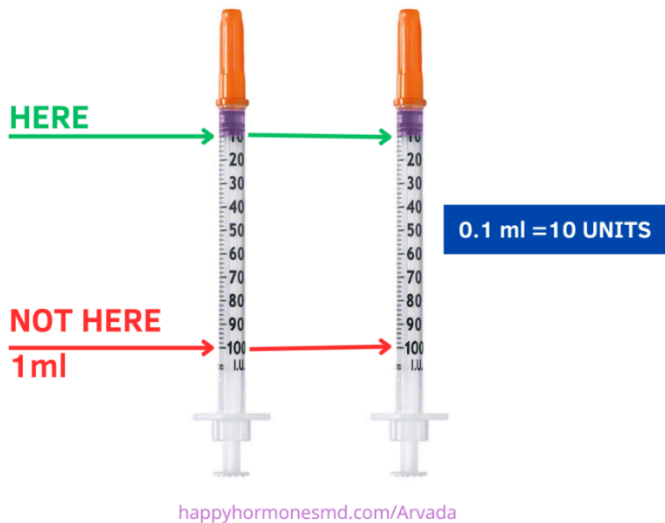
Dosing Schedule

Retatrutide - 10mg/ml

Weeks 1 and 2

Dose: 1mg

How much you inject: 0.1ml (or 10 units on insulin syringe) SQ once a week for 4 weeks

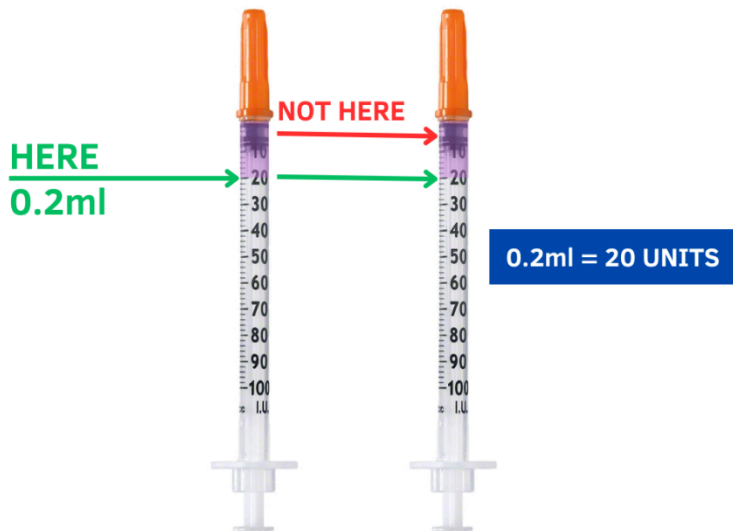


Weeks 3 through 6

Dose: 2mg

How much you inject: 0.2ml (or 20 units on insulin syringe) SQ once a week for 4 weeks

0.2ml - 20 units (Not 2 units)



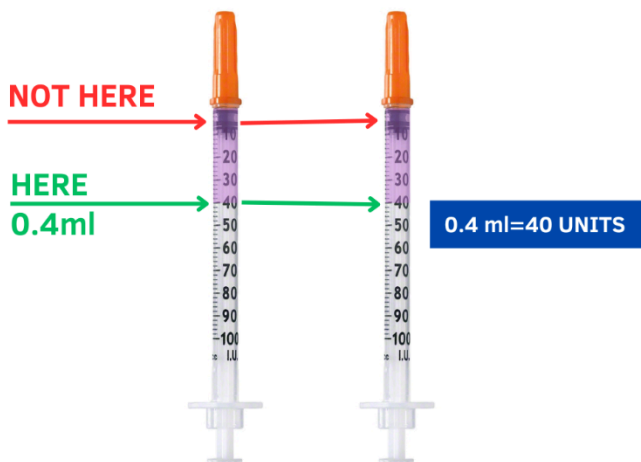
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Weeks 7 through 10

Dose: 4mg

How much you inject: 0.4ml (or 40 units on insulin syringe) SQ once a week for 4 weeks

0.4ml - 40 units (Not 4 UNITS)



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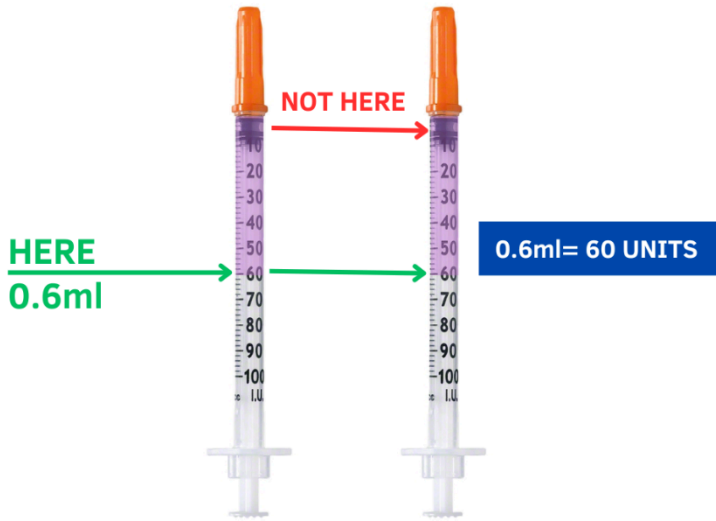
Weeks 11 through 14

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Dose: 6mg

How much you inject: 0.6ml (or 60 units on insulin syringe) SQ once a week for 4 weeks

0.6ml - 60 units (Not 6 units)



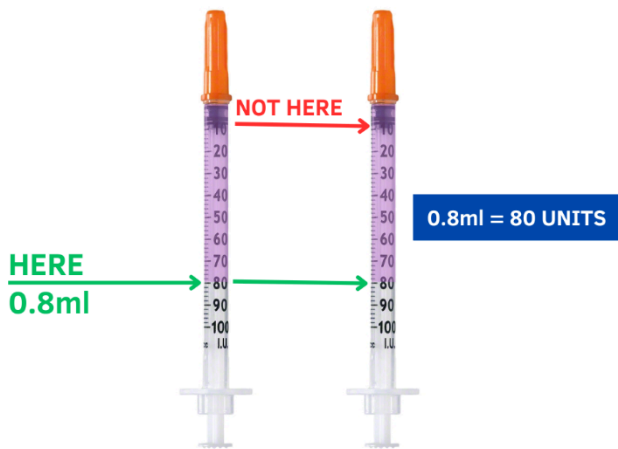
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Weeks 15 and on

Dose: 8mg

How much you inject: 0.8ml (or 80 units on insulin syringe) SQ once a week. This is the maximum dose.

0.8ml - 80 units (Not 8 units)



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