TIRZEPATIDE Protocol
Initial, Maintenance, Microdose

What is Tirzepatide?

- Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist. It is an amino acid sequence including a C20 fatty diacid moiety that enables albumin binding and prolongs the half-life.
  - Tirzepatide selectively binds to and activates both the GIP and GLP-1 receptors, the targets for native GIP and GLP-1.
    - As a GLP-1 receptor agonist that is in a class of medications called incretin mimetics.
    - GLP-1 is a physiological regulator of appetite and caloric intake. Nonclinical studies suggest the addition of GIP may further contribute to the regulation of food intake
- Tirzepatide is the active ingredient for weight loss and diabetic medications and is typically received by subcutaneous (SQ or Sub-Q) weekly injection.
- Tirzepatide lowers blood glucose levels – Tirzepatide works to lower high blood sugar by assisting the pancreas, mimicking a hormone called glucagon-like peptide 1 (GLP-1), (which controls the flow of glucose into cells) and increasing the amount of insulin that is released. These workings, in turn, lower the amount of glucagon released and delays gastric emptying. Insulin helps move sugar from the blood into other body tissues where it is used for energy. As a result, Tirzepatide:
  - Slows down movement of food through the stomach and stomach emptying so that, after eating, clients feel full longer.
  - Suppresses appetite and food cravings, reducing the amount of food clients will want to eat at a given sitting (on average clients eat ~30% less).

What is Tirzepatide used for?

- Tirzepatide is typically indicated in chronic weight management as an adjunct to
  - reduced calorie diet and
  - increased physical activity
  - For **Chronic Weight Management** in adult clients with an initial BMI of
    - 30 kg/m^2 or greater (obesity) or
    - 25 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, Type 2 diabetes mellitus, or dyslipidemia).
  - **For MAINTENANCE and MICRODOSE- the absolute lowest BMI allowed for a GLP1 injection is 21.**
    - At any time the client may be switched to SL GLP1s which do not have a BMI restriction
    - **Maintenance** means the lowest effective dose the patient can take and maintain a BMI of 23+
      - Once the BMI is below 23 the client is tapered to a MICRODOSE which is defined as 2.5mg or less of Tirzepatide
    - **Microdose** means dosing below 2.5mg total weekly
      - **BMI 21-23**-may be split into a twice weekly dose to manage cravings and reduce side effects

- Patient population benefit
  - Going through hormonal changes- menopause, perimenopause, and “mano-pause”
  - Managing cravings for food and alcohol
  - Needing to lose a small amount of weight effectively
  - Improve inflammation or inflammatory conditions
  - Failed other options such as phentermine, bella combo capsules, metformin, etc

What are Contraindications to getting Tirzepatide Injections?

- BMI below 21
  - Recommend SL GLP1s, Sermorelin, MIC shots, Carnitine Shots, ALA shots
- Prior adverse or allergic reaction to Tirzepatide, or to any of its ingredients (see inactive and other, such as Niacinamide etc)
- Prior history of anaphylaxis or angioedema with, or other adverse or allergic reactions to, another GLP-1 receptor agonist
  - Dulaglutide (Trulicity), Exenatide extended release (Bydureon Exenatide (Byetta), Liraglutide (Victoza, Saxenda), and Lixisenatide (Adlyxin).)
- Personal medical history involving:
  - Type 2 diabetes mellitus (the injection to be provided only under medical director’s discretion) and any related condition such as diabetic retinopathy (diabetic eye disease) or diabetic ketoacidosis.
    - Known HbA1C >8%
    - Disclose other Diabetic Medication
  - Type 1 diabetes mellitus
  - Pancreatitis
  - Gallbladder disease (unless uncomplicated removal of gallbladder has been performed- disclose to medical director).
  - Medullary Thyroid Carcinoma (MTC) thyroid cancer - Tirzepatide injection may increase the risk that client will develop tumors of the thyroid gland.
  - Multiple Endocrine Neoplasia, type 2 (MEN 2) glandular tumors.
  - Kidney disease/kidney insufficiency.
- Men or women trying to get pregnant (including the two-month period prior to the sexual or other activity ultimately resulting in pregnancy)
  - estimated background risk of major birth defects for offspring of clients attempting to become pregnant is approximately 6-10% of resulting pregnancies.
  - increased risk of miscarriage or pre-term birth for pregnancies in which the man or woman has received Tirzepatide

- Pregnant Women

- Clients who are breast-feeding / regularly engaged in breastfeeding a child (clients using Tirzepatide within two months prior to breast-feeding or at any time during the course of breast feeding will likely have Tirzepatide present in their breast milk)
- Clients who are less than 18 years old
- Tirzepatide is not administered while a person is receiving chemotherapy since one or more Tirzepatide IM/SQ injections may cause the chemotherapy to be less effective

Purpose
To establish compliant and legal guidelines for the administration of Tirzepatide for elective treatments. At no time, will any of these services be considered primary care services, nor shall its Medical Director, Registered Nurse or other licensed healthcare provider hold out to be performing as such. Services will be performed by the appropriately licensed individuals with clearly documented services and limitations.

Medical Director
The medical director is a credentialed physician who is responsible for overseeing all clinical aspects of operations. The medical director approves treatments and provisions and directs orders via direct communication, radio, phone, online, and the use of written protocols and standing orders.

Limitations
At no time will a provider operating under this protocol / standing order deviate from this protocol / standing order unless given documented permission by the medical director. In addition, at no time will a provider operating under this protocol / standing order administer a controlled substance. NOTE: All medications administered by non-prescribing providers are legend drugs (medications that can only be distributed by prescription) which do not carry the possibility of forming an addiction, whether they are FDA approved or not, Schedule III-V

Approval
The medical director has approved the following protocols.

Requirements
In compliance with state regulations, peptide will be administered by the client after training by a physician, APRN, or Physician Assistant who has been trained on the administering of peptides injections. Registered Nurses (RNs), Licensed Practical Nurse (LPNs),Licensed Vocational Nurses (LVNs), Emergency Medical Technicians (EMTs) and Paramedics may educate and train the client on administration of the peptides under the following criteria:
• The physician or APRN provides delegation and supervision, which may be accomplished remotely; and
• The RN, LPN, LVN, EMTs, Paramedics possesses the education, training, and skills required to teach administration of peptides safely and competently.

Procedure
1. **PRE-TREATMENT EVALUATION-** Prior to a client being administered a peptide, an assessment and telemedicine clearance must be performed on all consenting participants.

a. The assessment consists of obtaining the client's client's information via a patient encounter. This encounter can be in person or via video call. When the app is able to connect a Service Provider to a client then all documentation/communication must be done through the app.
    i. medical history
    ii. vital signs (blood pressure, heart rate, respirations, & pulse ox, temperature), mental alertness status
    iii. assessment of any change(s) in medical history / diagnosis- development of a new allergy, and whether the client is complaining about or experiencing any abnormal symptom(s) /illness(s)
    iv. BMI must be verified at 21 or higher
        1. 25+ Chronic Weight Management
        2. 23+ Maintenance
        3. 21+ Microdose

    v. Screening tool
b. Client/staff should complete the Tirzepatide screening tool, BMI Verification via in person or video call, and telehealth prior to receiving injection
    i. Clients who are currently on Tirzepatide elsewhere and are transferring to Hydreight
        1. Must establish care via intake and after telehealth, client may continue at the same dose they were previously on prior to transfer to Hydreight for initial fill of prescription.
            a. For subsequent fills and follow up dosing changes, follow protocol below as written.

c. Service Provider
    i. Educates the client re:
        1. Review the peptide information and education, what to expect
        2. How to give a subcutaneous injection
            a. Review video with patient
        3. Side effects of Tirzepatide
        4. If approved- Explain next steps such as prescription turn around time and scheduling
        5. Once the RX arrives the Client to record administration in the app
        6. Scheduling of follow ups after 3rd dose and every 4 weeks thereafter

d. Client should have completed via patient encounter with Service Provider:
        1. BMI- this is a calculation not a lab
e. Once clearance has been approved, the provider will approve patient-specific order thru app.
    i. Patient specific – this vial is ordered by the provider for the specific patient and is only to be used on this patient per the instructions on the label .

2. ADMINISTRATION OF TIRZEPATIDE – This is done by the client

a. Review the peptide information
b. Review video of Self administration of SQ injection
c. Client

i. Self-administers Tirzepatide per provided instructions and sig on the label
ii. Demonstrates in their training

d. Schedule follow up for after week 3 injection and then once monthly
e. Client instructed to Call for Questions, Problems, Adverse Reactions, and Concerns

3. **DOSING-** Given to men and women with
    a. 21+ BMI (PubMed Links: article 1, article 2, Peptide Sciences)
    b. Best to alternate between the left and right lower quadrants.
    c. Inject into abdomen once weekly.
        i. Chronic Weight Management BMI 25+
            1. Recommend for clients to start dosage at 2.5mg
            2. Titrate dose per dosing chart below every 4 weeks as tolerated or if weight plateaus.
                a. Client does not need to increase dosage if they are losing weight.
            3. Max dose is 15mg weekly.
        ii. Maintenance Dosing BMI 23-25
            1. Lowest effective dose weekly or twice weekly
            2. Emphasize lifestyle changes and management of cravings, alcohol consumption and tapering down in dosing to 2.5mg weekly or less
            3. May split dosing
            4. Client does not need to increase dosage if they are maintaining weight.
        iii. Microdosing BMI 21-23
            1. Less than 2.5mg weekly or split into twice weekly dosing
                a. Example:
                    i. Start at 0.25mg twice weekly
                    ii. May increase by 0.25mg to 0.5mg twice weekly
                    iii. Max is 1mg twice weekly
            2. Client does not need to increase dosage if they are maintaining weight.

4. **Follow Up/Maintenance –**
    a. Monthly Requirement-
        i. **BMI must be verified at 21 or higher by qualified Staff**
            1. BMI Determines Phase
                a. Weight Loss, Maintenance, Microdose
        ii. **Notes** should be made by the SP
            1. How is the patient doing?
            2. Are they losing weight?
            3. Are they maintaining?
            4. Which phase of dosing are they in?
            5. Side effects?
            6. Vitals?
        iii. If a dosing change is to be made a consultation must occur between the onsite medical service provider and the prescriber, unless the onsite service provider is the prescriber

1. **If NO dosing change is to be made AND the client is NOT due to see the HCP (Month 0,3, 6, 9 and so on), then the service provider may submit for another month, under the approval of the most recent HCP.**

Recommend Having Charts Handy

b. Every 3 months- **Consultation with HCP and patient is now required again. RE assessment required. Intake forms, BMI assessment via patient encounter**
   i. The assessment consists of obtaining the client's
      1. vital signs (blood pressure, heart rate, respirations, & pulse ox, temperature), mental alertness status
      2. Tirzepatide Re-Assessment Form
      3. assessment of any change(s) in medical history / diagnosis- development of a new allergy, and whether the client is complaining about or experiencing any abnormal symptom(s) /illness(s)
      4. **BMI must be verified at 21 or higher to determine dosing phase**
   ii. Retraining or Questions should be covered with HCP and onsite provider.

PerfectRx/Perfectionrx/Smartscripts (ships to all 50 states)- WEIGHT LOSS DOSING, MAINTENANCE

Month	MAX Weekly Dose	Vial sizes vary- 1,2,3ml 9mg/ml vials Tirzepatide 9mg/ml	Vials size in ml's	Number of vials
1	2.25mg	0.25ml (or 25 units)	1ml	1
2	4.5mg	0.5 ml (or 50 units)	2ml	1
3	6.75mg	0.75ml (or 75 units)	3ml	1
4	9mg	move to 18mg/ml vials		
5	11.25mg	move to 18mg/ml vials		
6	13.5mg	move to 20mg/ml vials		
7	15mg	move to 20mg/ml vials		

Month	MAX Weekly Dose	Vial sizes vary- 2,2.5,3ml, 4ml 18mg/ml Tirzepatide 18mg/ml	Vials size in ml's	Number of vials
1	2.25mg	use 9mg/ml vials		
2	4.5mg	use 9mg/ml vials		
3	6.75mg	use 9mg/ml vials		
4	9mg	18mg/ml vial-0.5 ml (or 50 units of 2ml vial)	2ml	1
5	11.25mg	18mg/ml vial-0.63ml (or 63 units)	2.5ml	1
6	13.5mg	18mg/ml vials- 0.75ml (75 units)	3ml	1
7+	15mg	18mg/ml vials- 0.83ml (or 83 units)	4ml	1

PerfectRx/Perfectionrx/Smartscripts (ships to all 50 states)-MICRODOSING- TITRATING DOWN ONLY IF NECESSARY

Month	MAX Dose	Vial sizes vary- 1ml 9mg/ml vials Tirzepatide 9mg/ml	Vials size in ml's	Number of vials
1	2mg weekly	0.22ml (or 22units)	1ml	1
2	1mg twice weekly	0.11 ml (or 11 units) twice weekly	1ml	1
3	1mg weekly	0.11 ml (or 11 units) weekly	1ml	1
4	0.5mg twice weekly	0.06 ml (6 units) twice weekly	1ml	1
5	0.5mg weekly	0.06 ml (6 units) weekly	1ml	1
6	0.25mg twice weekly	0.03 ml (3 units) twice weekly	1ml	1

PerfectRx/Perfectionrx/Smartscripts (ships to all 50 states)-MICRODOSING- TITRATING UP ONLY IF NECESSARY

Month	MAX Dose	Vial sizes vary- 1ml 9mg/ml vials Tirzepatide 9mg/ml	Vials size in ml's	Number of vials
1	0.25mg twice weekly	0.03 ml (3 units) twice weekly	1ml	1
2	0.5mg weekly	0.06 ml (6 units) weekly	1ml	1
3	0.5mg twice weekly	0.06 ml (6 units) twice weekly	1ml	1
4	1mg weekly	0.11 ml (or 11 units) weekly	1ml	1
5	1mg twice weekly	0.11 ml (or 11 units) twice weekly	1ml	1
6	2mg weekly	0.22ml (or 22units)	1ml	1

DiRx- WEIGHT LOSS DOSING, MAINTENANCE

Month	MAX Weekly Dose	Vial sizes: 2,4ml Tirzepatide 8.5mg, 17mg/B12 0.5mg/ml*	Vials size in ml's	Number of vials
1	2.125mg	Inject 2.125mg (25 Units) under the skin (SQ) once weekly.	2ml	1
2	4.25	Inject 4.25mg (50 Units) under the skin (SQ) once weekly.	2ml	1
3	6.75mg	Inject 6.75mg (40 Units) under the skin (SQ) once weekly.	2ml	1
4	9mg	Inject 9mg (53 Units) under the skin (SQ) once weekly.	4ml	1
5	11.25mg	Inject 11.25mg (66 Units) under the skin (SQ) once weekly.	4ml	1
6	13.5mg	Inject 13.5mg (79 Units) under the skin (SQ) once weekly.	4ml	1
7+	15mg	Inject 15mg (88Units) under the skin (SQ) once weekly.	4ml	1

DiRx- MICRODOSING- TITRATING DOWN ONLY IF NECESSARY

Month	MAX Weekly Dose	Vial sizes: 2,4ml Tirzepatide 8.5mg/B12 0.5mg/ml*	Vials size in ml's	Number of vials
1	2mg weekly	Inject 2mg (23 Units) under the skin (SQ) once weekly.	2ml	1
2	1mg twice weekly	Inject 1mg (11 Units) under the skin (SQ) twice weekly.	2ml	1
3	1mg weekly	Inject 1mg (11 Units) under the skin (SQ) once weekly.	2ml	1
4	0.5mg twice weekly	Inject 0.5mg (6 Units) under the skin (SQ) twice weekly.	4ml	1
5	0.5mg weekly	Inject 0.5mg (6 Units) under the skin (SQ) once weekly.	4ml	1
6	0.25mg twice weekly	Inject 0.25mg (3 Units) under the skin (SQ) twice weekly.	4ml	1

DiRx- MICRODOSING- TITRATING UP ONLY IF NECESSARY

Month	MAX Weekly Dose	Vial sizes: 2,4ml Tirzepatide 8.5mg/B12 0.5mg/ml*	Vials size in ml's	Number of vials
1	0.25mg twice weekly	Inject 0.25mg (3 Units) under the skin (SQ) twice weekly.	2ml	1
2	0.5mg weekly	Inject 0.5mg (6 Units) under the skin (SQ) once weekly.	2ml	1

3	0.5mg twice weekly	Inject 0.5mg (6 Units) under the skin (SQ) twice weekly.	2ml	1
4	1mg weekly	Inject 1mg (11 Units) under the skin (SQ) once weekly.	4ml	1
5	1mg twice weekly	Inject 1mg (11 Units) under the skin (SQ) twice weekly.	4ml	1
6	2mg weekly	Inject 2mg (23 Units) under the skin (SQ) once weekly.	4ml	1

5. WARNINGS/PRECAUTIONS

a. Use of tirzepatide may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying. This delay is largest after the first dose and diminishes over time. Advise patients using oral hormonal contraceptives to switch to a non-oral contraceptive method, or add a barrier method of contraception, for 4 weeks after initiation with tirzepatide and for 4 weeks after each dose escalation

6. ADVERSE REACTIONS

For a complete listing of adverse reactions, refer to the peptide package insert. The most common adverse reactions to Tirzepatide are injection site reactions (swelling, redness, bruising, pain, itching, infection) GI upset, diarrhea, constipation. Refer to Adverse Reactions SOP for any signs or symptoms concerning for adverse reaction.

Some Potential Adverse Reactions, Side Effects or Complications to Tirzepatide

Tremors*	Cramps*	Difficulty Breathing*
Flushes*	Anaphylaxis*	Angioedema*
Fainting/dizziness	Severe Headache	Vomiting
Diarrhea	Nausea	Irregular Hunger
Unexplained Anxiety	Unexplained Irritability	Irregular Weakness
Chills / Fever	Gauntness	Heart Rate Changes
Hypoglycemia	Dizziness	Retinopathy
Vision changes/impairment	Color blindness	Blurred vision
Abdominal pain	Constipation	Heartburn
Burping	Rash/Itching	Swelling of eyes, face, mouth
Jaundice	Stool discoloration	Swelling of legs, ankles, feet

* Denotes potential Tirzepatide toxicity (allergic hypersensitivity) – follow Emergency Protocol.

Some Symptoms to Thyroid Gland Tumors (Including MTC)

Swelling in neck / throat*	Hoarseness*	Difficulty Breathing*
Difficulty Swallowing*		

* Denotes potential for thyroid gland tumor – see our physician or other healthcare provider.

Some General SQ/IM Injection Side Effects or Complications		
Injection-Site Effects*	Headache	Nausea/Upset Stomach
Indigestion/Heartburn	Mild Diarrhea	Joint Pain
Vein Inflammation	Lightheadedness	Increased Thirst
Dizziness	Chills	Severe Fatigue
Infection	Fever	Shakes

* Injection-site effects may include, without limitation, temporary pain, burning, bruising, blood, cellulitis or discoloration at the site of injection.

7. **Emergency Protocol**
    - **a.** Client to proceed, or if necessary client to be sent, to the emergency room at a local hospital; OR
    - **b.** Client to proceed, or if necessary client to be sent, to local urgent care center; OR
    - **c.** Client to call, or if necessary call on behalf of client, 9-1-1 emergency telephone number; OR
    - **d.** Client to call, client's regular, independent physician or other qualified healthcare provider
    - **e.** See Post-Emergency Protocol Below also.

8. **Post-Emergency Protocol** – After the Emergency Protocol,
    - **a.** Client to service provider, and service provider will prepare and complete an incident report by phone to be submitted on the app under specific client profile.
    - **b.** If the client does not complete a report, business partner or associate partner then will coordinate completion of relevant portions of the report with its Medical Director without client input.
    - **c.** Final incident report shall be submitted directly to the medical director email, and thru the app.

9. **DISCONTINUING TIRZEPATIDE:**
    - **a.** Client falls below BMI of 21
    - **b.** Schedule telehealth with Medical Provider
    - **c.** Medical provider will Place client on taper off of Tirzepatide
        - **i. Can transition patient to support options**
            1. **MIC (methionine/inositol/choline) containing products**
            2. **Drip support**
            3. **Sermorelin**
    - **d.** Continue to follow implemented lifestyle changes
        - **i.** Diet, exercise, counseling
    - **e.** Warn of return of
        - **i.** Pretreatment appetite
        - **ii.** Increase in gastric emptying
        - **iii.** Increase in blood glucose
    - **f.** Options to move to other weight loss support

i. MIC injections
ii. Drips etc
iii. Sermorelin

Resources

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217806s000lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215866s000lbl.pdf