TIRZEPATIDE Protocol

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
  - 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).
    - See below regarding calculation of BMI.

What are Contraindications to getting Tirzepatide Injections?

- 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
    - Clients who are experiencing or have experienced depression with a history of suicidal attempts, suicidal thoughts or active suicidal ideation.
    - 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
    - Tirzepatide is not co-administered with sermorelin. Tirzepatide is for patients with a BMI greater than 25 with the above indications. Sermorelin is medically appropriate for individuals who are otherwise relatively healthy with 5-15 pounds to lose and at a lower BMI.

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 25 or higher in person or via video call/app
        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. 25+ 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. Recommend for clients to start dosage at 2.5mg
        ii. Titrate dose per dosing chart below every 2-4 weeks as tolerated or if weight plateaus.
            1. Client does not need to increase dosage if they are losing weight.
        iii. Max dose is 15mg weekly.

4. **Follow Up/Maintenance –**
    a. Monthly Requirement-
        i. **BMI must be verified at 25 or higher by Hydreight Service Provider**
        ii. **Notes** should be made by the SP
            1. How is the patient doing?
            2. Are they losing weight?
            3. Side effects?
            4. Vitals?

iii. **If a dosing change is to be made a consultation must occur between the SP and the HCP**
    1. Recommend Handing out the chart below
iv. **Empower all states except Cali, Wisconsin, Iowa**
    1. **SP must go out at week 3 and then monthly**
    2. **Has 3 vials- see charts for preferred vial for month they are on**
v. **California- Redrock (select states) There are 2 strengths (8.5mg and 17mg/ml) and 6 vial sizes**
    1. Tirzepatide 8.5mg/ml – 1ml, 2ml, 3ml vial (total 8.5mg, 17mg, 25.5mg, of Tirzepatide)
vi. **Southend (All states except AL, AR, CA, NC, NJ, NE, NV, MD, SC)**
    1. **SP must go out at week 3 and then monthly**
    2. **2 vial strengths and 7 vial sizes-see charts for preferred vial per month**

b. Every 3 months- **Consultation with HCP 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 25 or higher**
    ii. Retraining or Questions should be covered with HCP and SP.

Empower (All states except Cali, Wisconsin, Iowa There are 2 vial strengths and 3 vials. Once punctured, the vial is to be discarded at 28 days.
Tirzepatide 8mg/Niacinamide 2mg/ml 2.5ml vial (total 20mg of Tirzepatide) (used when client is on 2.5mg and 5mg)
Tirzepatide 17mg/Niacinamide2mg/ml 2ml vial (total 34mg of Tirzepatide) (used when client is on 7.5mg)
Tirzepatide 17mg/Niacinamide2mg/ml 4ml vial (total 34mg of Tirzepatide) (used when client is on 10mg, 12.5mg and 15mg)

Month	MAX Weekly Dose	Lower Strength Vial 2.5ml Tirzepatide 8mg/Niacinamide 2mg/ml	Number of vials
1	2.5mg	0.31ml (or 31 units of 20mg vial)	1
2	5mg	0.63 ml (or 63 units of 20mg vial)	1
3	7.5mg	0.94 ml (or 94 units of 20mg vial)	2
4	10mg	move to higher strength vial	-
5	12.5mg	move to higher strength vial	-
6+	15mg	move to higher strength vial	-

****Reminder: Client does not need to increase dosage if they are losing weight. ****

Month	MAX Weekly Dose	Higher Strength 2ml Vial 2ml Tirzepatide 17mg/Niacinamide 2mg/ml	Number of vials
1	2.5mg	0.15ml (or 15 units of 34mg vial)	1
2	5mg	0.29 ml (or 29 units of 34mg vial)	1
3	7.5mg	0.44ml (or 44 units of 34mg vial)	1
4	10mg	0.59 ml (or 59 units of 34mg vial) OR move to higher volume vial	2
5	12.5mg	0.74ml (or 74 units of 34mg vial) OR move to higher volume vial	2
6+	15mg	0.88 ml (or 88 units of 34mg vial) OR move to higher volume vial	2

****Reminder: Client does not need to increase dosage if they are losing weight. ****

Month	MAX Weekly Dose	Higher Strength 4ml Vial 4ml Tirzepatide 17mg/Niacinamide 2mg/ml	Number of vials
1	2.5mg	0.15ml (or 15 units of 68mg vial)	1
2	5mg	0.29 ml (or 29 units of 68mg vial)	1
3	7.5mg	0.44ml (or 44 units of 68mg vial)	1
4	10mg	0.59 ml (or 59 units of 68mg vial)	1
5	12.5mg	0.74ml (or 74 units of 68mg vial)	1
6+	15mg	0.88 ml (or 88 units of 68mg vial)	1

****Reminder: Client does not need to increase dosage if they are losing weight. ***

OR

Redrock (Ships to 47 states- except- AR, LA, NJ) There are 2 strengths (8.5mg and 17mg/ml) and 7 vial sizes

Tirzepatide 8.5mg/ml – 1ml, 2ml, 3ml vial (total 8.5mg, 17mg, 25.5mg, of Tirzepatide) used per the dosing chart below

Month	MAX Weekly Dose	Vial sizes vary- 1,2,3,ml 8.5mg/ml vials Tirzepatide 8.5mg/ml Glycine 5mg/ml	Vials size in ml's	Number of vials
1	2.125mg	0.25ml (or 25 units of 1ml vial)	1ml	1
2	4.25mg	0.5 ml (or 50 units of 2ml vial)	2ml	1
3	6.375mg	0.75ml (or 75 units of 3ml vial)	3ml	1
4	8.5mg	use 17mg/ml 2ml vial		
5	11mg	use 17mg/ml 3ml vial		
6	13.5mg	use 17mg/ml 3.5ml vial		

7+	15mg	0.9ml (or 90 units of 4ml vial	4ml	1

Month	MAX Weekly Dose	Vial sizes vary- 1,2,3,ml 8.5mg/ml vials Tirzepatide 8.5mg/ml B12 500mcg/ml	Vials size in ml's	Number of vials
1	2.125mg	0.25ml (or 25 units of 1ml vial)	1ml	1
2	4.25mg	0.5 ml (or 50 units of 2ml vial)	2ml	1
3	6.375mg	0.75ml (or 75 units of 3ml vial)	3ml	1
4	8.5mg	use 17mg/ml 2ml vial		
5	11mg	use 17mg/ml 3ml vial		
6	13.5mg	use 17mg/ml 3.5ml vial		
7+	15mg	use 17mg/ml 4ml vial		

Tirzepatide 17mg/ml – 2ml, 2.5ml, 3ml vial (total 40mg, 50mg, 60mg, of Tirzepatide) used per the dosing chart below

Month	MAX Weekly Dose	Vial sizes vary- 2, 3, 3.5, 4ml 17mg/ml vials Tirzepatide 17mg/ml Glycine 5mg/ml	Vials size in ml's	Number of vials
1	2.125mg	Use 8.5mg/ml vial		
2	4.25mg	Use 8.5mg/ml vial		
3	6.375mg	Use 8.5mg/ml vial		
4	8.5mg	0.5ml (or 50 units of 2ml vial)	2ml	1
5	11mg	0.65ml (or 65 units of 2.5ml vial)	3ml	1
6+	13.5mg	0.8ml (or 80 units of 3ml vial)	3.5ml	2
7+	15mg	0.9ml (or 90 units of 4ml vial	4ml	1

Month	MAX Weekly Dose	Vial sizes vary- 2, 3, 3.5, 4ml 17mg/ml vials Tirzepatide 17mg/ml B12 500mcg/ml	Vials size in ml's	Number of vials
1	2.125mg	Use 8.5mg/ml vial		
2	4.25mg	Use 8.5mg/ml vial		
3	6.375mg	Use 8.5mg/ml vial		
4	8.5mg	0.5ml (or 50 units of 2ml vial)	2ml	1
5	11mg	0.65ml (or 65 units of 3ml vial)	3ml	1

6	13.5mg	0.8ml (or 80 units of 3.5ml vial)	3.5ml	1
7+	15mg	0.9ml (or 90 units of 4ml vial	4ml	1

Southend (Ship to all but- AL, AR, CA, MD, MA, NE, NV, NJ,NC, SC)– There is 1 vial strength and 2 vial sizes.

Tirzepatide 22mg/ml, 1ml. Used per dosing charts below. Medical Necessity will be required and documented by the prescriber to move the prescription forward.

Month	MAX Weekly Dose	Vial sizes vary- 1ml 22mg/ml vials Tirzepatide 22mg/ml Pyridoxine 4mg/ml	Vials size in ml's	Number of vials
1	2.2mg	0.1ml or 10 units	1ml	1
2	4.4mg	0.2ml or 20 units	1ml	1
3	6.6mg	0.3ml or 30 units	2ml	2x1ml
4	8.8mg	0.4ml or 40 units	2ml	2x1ml
5	11mg	0.5ml or 50 units	2ml	2x1ml
6+	13.2mg	0.6ml or 60 units	3ml	3x1ml

IF split dosing is medically necessary per prescriber

Month	MAX Weekly Dose	Vial sizes vary- 1ml 22mg/ml vials Tirzepatide 22mg/ml Pyridoxine 4mg/ml	Vials size in ml's	Number of vials
1	2.2mg	0.05ml or 5 units twice weekly	1ml	1
2	4.4mg	0.1ml or 10 units twice weekly	1ml	1
3	6.6mg	0.15ml or 15 units twice weekly	2ml	2x1ml
4	8.8mg	0.2ml or 20 units twice weekly	2ml	2x1ml
5	11mg	0.25ml or 25 units twice weekly	2ml	2x1ml
6+	13.2mg	0.3ml or 30 units twice weekly	3ml	3x1ml

7 Cells (Ships to 44 states- except- AR, AL, MS, CA, IN, SC) There are 4 vial strengths see chart below.

Month	MAX Weekly Dose	Vial size 2ml 1mg/ml, 2mg/ml, 4mg/ml, 5mg/ml Tirzepatide 5, 10, 15, 25, 30mg/ml B3 0.33, 0.66, 1, 1.66, 2mg/ml	Vials size and strength	Number of vials
1	2.5mg	0.5 ml (or 50 units)	5mg/0.33mg/mL (2ml vial)	1
2	5mg	0.5 ml (or 50 units	10mg/0.66mg/mL (2ml vial)	1

3	7.5mg	0.5 ml (or 50 units)	15mg/1mg/mL (2ml Vial)	1
4	10mg	1ml (or 100 units)	10mg/0.66mg/mL (4ml vial)	1
5	12.5mg	0.5 ml (or 50 units)	25mg/1.66mg/mL (2ml vial)	1
6+	15mg	0.5 ml (or 50 units	30mg/2mg/mL (2ml Vial)	1

PerfectRx/Perfectionrx/Smartscripts (ships to all 50 states)

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

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 25
    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