SEMAGLUTIDE Protocol

What is Semaglutide?

- Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that is in a class of medications called incretin mimetics.
- Semaglutide is the active ingredient for weight loss and diabetic medications and is typically received by subcutaneous (SQ or Sub-Q) weekly injection.
- Semaglutide lowers blood glucose levels – Semaglutide 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, Semaglutide:
    - 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 Semaglutide used for?

- Semaglutide 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 Semaglutide Injections?

- Prior adverse or allergic reaction to Semaglutide, or to any of its ingredients (see inactive and other, such as B12, carnitine 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:
    - 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 - Semaglutide 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 3% of resulting pregnancies.
        - estimated background risk of miscarriage for pregnancies in which the man or woman has received Semaglutide is approximately 18% of such resulting pregnancies.
    - Pregnant women

        - Clients who are breast-feeding / regularly engaged in breastfeeding a child (clients using Semaglutide within two months prior to breast-feeding or at any time during the course of breast feeding will likely have Semaglutide 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.
    - Semaglutide is not administered while a person is receiving chemotherapy since one or more Semaglutide IM/SQ injections may cause the chemotherapy to be less effective
    - Semaglutide is not co-administered with sermorelin. Semaglutide 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 Semaglutide 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 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 Semaglutide screening tool, BMI Verification via in person or video call, and telehealth prior to receiving injection
        i. Clients who are currently on Semaglutide 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 semaglutide
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 SEMAGLUTIDE – 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 semaglutide 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 0.25mg
      ii. Titrate dose per dosing chart below every 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 2.5mg 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. Mississippi-ANAZAO ONLY
      MONTH 1 and MONTH(S) client maybe changing from 0.5mg to 0.75mg
         1. SP must go out on week 3 for Follow Up/Maintenance

a. If client stays at 0.5mg, plan visit for week 3 again following month.

b. If client increases to 0.75mg- explain change to strength and potency of their vial and how they will inject less but get more drug.

i. Use dosing chart below under "Anazao"

v. Alabama- EMPOWER ONLY

1. Note there are 4 vials and when patient changes dose they likely change vials
    a. SP MUST educate on change from 1mg/ml to 5mg/ml

vi. **Hallandale all states except - CA, MN, MI, KS, AR, AL, HI**

1. SP must go out at week 3 and then monthly

2. Has 4 vials- see charts for preferred vial for month they are on

vii. California- Tailor Made ONLY

1. Note there are 2 vials and when patient changes dose from 0.5mg to 1mg they change vial strength
    a. SP MUST educate on change from 1mg/ml to 5mg/ml

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. Semaglutide 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.

PQ Pharma (All but CA) There are 2 vial strengths and 5 vials. Once punctured, the vial is to be discarded at 28 days.

Semaglutide 1mg/ ml 1ml vial (total 1mg of semaglutide) (used when client is on 0.25mg)

Semaglutide 2.5mg/ml 1ml vial (total 2.5mg of semalgutide) (used when client is on 0.5mg)

Semaglutide 2.5mg/ml 2ml vial (total 5mg of semaglutide) (used when client is on 1mg)

Semaglutide 2.5mg/ml 3ml vial (total 7.5mg of semaglutide) (used when client is on 1.7mg)

Semaglutide 2.5mg/ml 4ml vial (total 10mg of semaglutide) (used when client is on 2.4mg)

Once punctured, the vial is to be discarded at 28 days.

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

Month	MAX Weekly Dose	Lower Strength Vial Semaglutide 1mg/ml	Higher Strength Vials Semaglutide 2.5mg/ml	Vial Size
1	0.25mg	0.25ml (25 units of 1mg, 1ml vial)		1ml
2	0.5mg	move to 2.5mg/ml, 1ml vial	0.2ml (20 units of 2.5mg/ml)	1ml
3	1mg	move to 2.5mg/ml, 2ml vial	0.4ml or (40 units of 2.5mg/ml)	2ml
4	1.7mg	move to 2.5mg/ml, 3ml vial	0.68ml or (68 units of 2.5mg/ml)	3ml
5 +	2.4mg	move to 2.5mg/ml, 4ml vial	0.96ml or (96 units of 2.5mg/ml)	4ml

Olympia (all state but AL, CA, MS)– There is 1 vial strength and sizes.

Semaglutide 5mg/ml and a 3ml vial (total 15mg of semaglutide)

Once punctured, the vial is to be discarded at 28 days.

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

Month	MAX Weekly Dose	ONLY ONE VIAL STRENGTH 3ml Semaglutide 5mg/ml	Number of Vials
1	0.25mg	0.05ml (5 units of vial)	1-prefer a smaller vial/different vendor
2	0.50mg	0.1ml (10 units of vial)	1-prefer a smaller vial/different vendor
3	1.00mg	0.2 ml (or 20 units of vial)	1
4	1.75mg	0.35ml (or 35 units of vial)	1
5+	2.5mg	0.5ml (or 50 units of vial)	1

*Medical provider to order 2 vials when patient goes from 1mg weekly dose to 1.75mg

Empower (AL) There are 2 vial strengths and 4 vials. Once punctured, the vial is to be discarded at 28 days.

Semaglutide 1mg/B12 0.5mg/ml 1ml vial (total 1mg of semaglutide) (used when client is on 0.25mg)

Semaglutide 1mg/B12 0.5mg/ml 2.5ml vial (total 2.5mg of semalgutide) (used when client is on 0.5mg)

Semaglutide 5mg/ B12 0.5mg/ml 1ml vial (total 5mg of semaglutide) (used when client is on 1mg)

Semaglutide 5mg/ B12 0.5mg/ml 2.5ml vial (total 12.5mg of semaglutide) (used when client is on 1.7mg, 2.4mg and above)

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

Month	MAX Weekly Dose	Lower Strength Vial Semaglutide 1mg/B12 0.5mg	Higher Strength Vial Semaglutide 5mg/B12 0.5mg
1	0.25mg	0.25ml (25 units of 1mg-1ml vial)	
2	0.5mg	0.50 ml (or 50 units of 1mg-2.5ml vial)	
3	1mg	Move to higher strength vial	0.20ml or (20 units of 5mg-1ml vial)
4	1.7mg	move to higher strength vial	0.34ml or (34 units of 5mg-2.5ml vial)
5 +	2.4mg	move to higher strength vial	0.48ml or (48 units of 5mg-2.5ml vial)

Hallandale all states except - CA, MN, MI, KS, AR, MS, AL, HI- There is 1 strength and 4 vial sizes

Semaglutide 2.5mgm/ml – 1ml, 2ml, 3ml, 5ml vial (total 2.5mg,5mg, 7.5mg, 12.5mg of Semaglutide) used per the dosing chart below

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

Month	MAX Weekly Dose	Vial sizes vary- 1,2,3,5ml 2.5mg/ml vials Semaglutide 2.5mg/ml	Vials size in ml's	Number of vials
1	0.25mg	0.1ml (or 10 units of 1ml vial)	1ml	1
2	0.5mg	0.2 ml (or 20 units of 1ml vial)	1ml	1
3	1mg	0.4ml (or 40 units of 1 or 2ml vial)	1ml vial or 2ml vial	1 or 2
4	1.7mg	0.68ml (or 68 units of 3ml vial)	3ml	1
5+	2.5mg	1ml (or 100 units)	5ml	1

Tailor Made (CA)- There are 2 vial strengths. Once punctured, the vial is to be discarded at 28 days.

Semaglutide 5mg/B12 0.4mg/ml 1ml vial (total 5mg of semaglutide) (used when client is on 0.25mg, 0.5mg)

Semaglutide 5mg/B12 0.4mg/ml 2ml vial (total 10mg of semaglutide) (used when client is on 1mg and above)

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

Month	MAX Weekly Dose	Lower Strength Vial **Semaglutide 5mg/B12 0.4mg/1ml-1ml vial**	Higher Strength Vial **Semaglutide 5mg/B12 0.2mg/ml-2ml vial**
1	0.25mg	0.05ml (5 units of 1ml vial)	
2	0.5mg	0.1 ml (or 10 units of 1ml vial)	
3	1mg	0.20ml or (20 units of 5mg/ml 1ml vial)	
4	1.7mg	move to higher volume vial	0.34ml or (34 units of 5mg/ml vial)
5 +	2.4mg	Move to higher volume strength vial	0.48ml or (48 units of 5mg/ml vial)

OR

Redrock (select states) There is 1 strength and 3 vial sizes

Semaglutide 2.5mgm/ml – 1ml, 2ml, 4ml vial (total 2.5mg,5mg, 10mg, of Semaglutide) used per the dosing chart below

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

Month	MAX Weekly Dose	Vial sizes vary- 1,2,4ml 2.5mg/ml vials **Semaglutide 2.5mg/ml**	Vials size **in ml's**	Number of **vials**
1	0.25mg	0.1ml (or 10 units of 1ml vial)	1ml	1
2	0.5mg	0.2 ml (or 20 units of 1ml vial)	1ml	1
3	1mg	0.4ml (or 40 units of 2ml vial)	2ml	1
4	1.7mg	0.68ml (or 68 units of 3ml vial)	4ml	1
5 +	2.5mg	1ml (or 100 units)	4ml	1

OR

Southend (All states except AL, AR, CA, NC, NJ, NE, NV, MD, SC) There are 2 strengths and 3 vial sizes.
Semaglutde 1mg/ml Pyridoxine 8mg/ml- 1ml vial and semaglutide 5mg/ml pyridoxine 8mg/ml 1ml and 2ml vial

Month	MAX Weekly Dose	1ml vial Semaglutide 1mg/ml Pyridoxine 8mg/ml	Vials size in ml's	Number of vials
1	0.25mg	0.25ml (or 25 units)	1ml	1
2	0.5mg	0.5 ml (or 50 units	1ml	2
3	1mg	Go to higher strength		
4	1.7mg	Go to higher strength		
5+	2.5mg	Go to higher strength		

Month	MAX Weekly Dose	Vial sizes vary- 1,2ml 5mg/ml vials Semaglutide 5mg/ml Pyridoxine 8mg/ml	Vials size in ml's	Number of vials
1-Jan	0.25mg	Use lower strength		
2	0.5mg	0.1 ml (or 10 units)	1ml vial	1
3	1mg	0.2ml (or 20 units)	1ml vial	1
4	1.7mg	0.34ml (or 34 units)	2ml vial	1
5+	2.5mg	0.48ml (or 48units)	2ml vial	1

5. WARNINGS/PRECAUTIONS

a. Use of Semaglutide 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 Semaglutide 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 Semaglutide 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 Semaglutide

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 Semaglutide 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 SEMAGLUTIDE:

a. Client falls below BMI of 25

b. Schedule telehealth with Medical Provider

c. Medical provider will Place client on taper off of Semaglutide

i. Can transition patient to support options

1. MIC (methionine/inositol/choline) containing products

2. Drip support

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

Resources

- Micromedex Drug Detail re Semaglutide – Drugdex Evaluations dated 2/14/23.
- https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf
- NOVOMEDLINK. Obesity. (2022). https://www.novomedlink.com/obesity/hcp-education/treatment-guidelines/aace-guidelines.html
- Ojeniran, M., Dube, B., Paige, A., Ton, J., & Lindblad, A. J. (2021). Semaglutide for weight loss. *Canadian family physician Medecin de famille canadien*, *67*(11), 842. https://doi.org/10.46747/cfp.6711842
- Newsome, Philip N., et als., A Placebo-Controlled Trial of Subcutaneous Semaglutide in Nonalcoholic Steatohepatitis. *New England Journal of* Medicine, 384:1113-1124 https://www.nejm.org/doi/full/10.1056/NEJMoa2028395
- American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines For Medical Care of Patients with Obesity (2022). **https://www.endocrinepractice.org/article/S1530-891X(20)44630-0/fulltext**
- https://pubmed.ncbi.nlm.nih.gov/32359762/