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Practice Policy and Guidelines for Compounded GLP-1 Drugs

The FDA recently issued warning regarding unapproved compounded GLP-1 drugs-specifically semaglutide and tirzepatide marked for weight loss (brand names include: Ozempic, Zepbound, Mounjaro and Wegovy**).** These GLP-1 medications **have not** been evaluated for safety or effectiveness raising significant concerns about their overall quality and risks to patients.

Key Concerns:

- Unapproved Status: Compounded GLP-1 drugs do not undergo the rigorous FDA review process for safety and efficacy which raises serious health risks for consumers.

- Misleading Advertising: The FDA is actively addressing misleading claims made by telehealth companies and other marketers regarding these drugs. Many advertisements imply that compounded versions are equivalent to FDA-approved products which is not the case.

- Quality Issues: There have been reports of compounded GLP-1 drugs arriving warm or improperly shipped/stored which can compromise their quality. The FDA advises against using any injectable GLP-1 drugs that do not meet proper storage/shipping conditions.

Please be advised that St. Michael Medical Clinic maintains no ownership or affiliate relationship with any compounding facility. It is the patient's sole responsibility to ensure that their selected compounding pharmacy utilizes approved techniques and verified ingredients. Unlike FDA-approved drugs, compounded medications are not reviewed by the FDA for safety or efficacy before they reach patients. We encourage all patients to confirm their pharmacy is accredited by the PCAB or a similar recognized body.

We are providing you a tailored prescription to support your journey towards a healthier you. To achieve the best results, it is essential to be proactive with your daily habits, such as choosing nutritious foods and increasing your physical activity. By combining this treatment with a healthy lifestyle, you are much more likely to reach and maintain your wellness goals.

By signing below, you acknowledge the following:

- **Informed Consent:** I have been fully briefed on the potential side effects and significant risks associated with GLP-1 therapy. I have read the provided documentation and voluntarily accept the risks.
- **Reporting Obligation:** I agree to disclose all medical issues or concerns to the clinical team immediately.
- **Adherence to Follow-Up:** I understand that continued treatment is contingent upon attending MONTHLY follow up appointments during the titration period and QUARTERLY appointments thereafter for longterm efficacy, safety and progress.

Patient Name:_____ DOB:_____

Patient Signature:_____ Date:_____

St. Michael Medical Clinic Staff Witness: ____ [date imported to pt chart: _____]

FOR YOUR INFORMATION Side effect of meds (Not all inclusive)

Please check with manufacturer site

Side Effect of Rybelsus, Ozempic, Wegovy (Semaglutide): oral tablet, subcutaneous solution

Warning: Risk of Thyroid C-Cell TumorsIn rodents, semaglutide causes thyroid C-cell tumors. It is unknown whether semaglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. Semaglutide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors

General

The most commonly reported adverse reactions have included nausea, vomiting, diarrhea, abdominal pain, and constipation. [Ref]

Oncologic

GLP- 1 Receptor Agonist:

Postmarketing reports: Medullary thyroid cancer

Cases of Medullary thyroid cancer (MTC) have been reported in patients treated with liraglutide in the postmarketing period; the data in these reports is insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

Gastrointestinal

Very common (10% or more): Nausea (up to 44%), increased amylase (up to 13%), increased lipase (up to 22%), diarrhea (up to 30%), vomiting (up to 24%), constipation (up to 24%), abdominal pain (up to 20%),
Common (1% to 10%): Dyspepsia, eructation, flatulence, gastroesophageal reflux disease, abdominal distention, gastroenteritis, gastroesophageal reflux disease, gastritis, gastroenteritis (viral)
Uncommon (0.1% to 1%): Appendicitis

Frequency not reported: Acute and necrotizing pancreatitis, chronic pancreatitis

In clinical trials for type 2 diabetes, acute pancreatitis was confirmed by adjudication in 7 (0.3 cases per 100 patient years) and 8 patients (0.27 per 100 patient years) in 2 separate trials (compared to 3 and 10 placebo treated patients, respectively). One case of chronic pancreatitis was confirmed. In clinical trials for weight loss, 4 cases of acute pancreatitis were confirmed by adjudication (vs 1 placebo case). In weight loss trials, nausea, diarrhea, vomiting, constipation, and abdominal pain were reported more frequently than in clinical trials for type 2 diabetes.

Hypersensitivity

Rare (less than 0.1%): Anaphylactic reaction
Frequency not reported: Angioedema
Postmarketing reports: Ananaphylaxis, rash, urticaria

Ocular

In a 2-year trial among patients with type 2 diabetes and high cardiovascular risk, patients treated with this drug experienced a great incidence of diabetic retinopathy complications (3% vs 1.8%). The absolute risk was greater in patients with a history of diabetic retinopathy at baseline (8.2%[drug] vs 5.2%[placebo]) than those without (0.7%[drug] vs 0.4%[placebo]).

Common (1% to 10%): Diabetic retinopathy complications

Metabolic

Very common (10% or more): Hypoglycemia (up to 30% when used in combination with basal insulin)
Common (1% to 10%): Hypoglycemia, decreased appetite, weight loss
In the weight loss clinical trials, patients without type 2 diabetes experienced episodes of hypoglycemia.

Local

Common (1% to 10%): Injection site reactions

Immunologic

Frequency not reported: Development of anti-semaglutide (the active ingredient contained in Ozempic) antibodies

As with other protein and peptide pharmaceuticals, patients receiving this drug have developed anti-semaglutide antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay, as well as other factor in handling of the sample. For these reasons, the incidence of antibodies cannot be directly compared with other products. Anti-drug antibodies to semaglutide have been reported in up to 1% of patients during clinical trials.

Hepatic

Common (1% to 10%): Cholelithiasis
Uncommon (0.1% to 1%): Cholecystitis
Frequency not reported: Acute gallbladder disease
Cholelithiasis has been reported in 1.5% and 0.4% of patients receiving 0.5 mg and 1 mg weekly, respectively.

Other

Very common (10% or more): Fatigue (up to 11%)
Fatigue was reported in greater than 0.4% of patients.

Nervous system

Very common (10% or more): Headache (up to 14%)
Common (1% to 10%): Dizziness
Uncommon (0.1% to 1%): Dysgeusia

Renal

Postmarketing reports: Acute kidney injury, worsening of chronic renal failure

Cardiovascular

A mean increase in heart rate of 2 to 3 beats per minute (bpm) was reported in clinical trials for type 2 diabetes. In weight loss clinical trials, a mean increase in resting heart rate of 1 to 4 bpm was observed. Maximal changes from baseline at any visit of 10 to 19 bpm (41% vs 34% placebo) and 20 bpm (26% vs 16% placebo) were recorded. In weight loss clinical trials, Hypotension and orthostatic hypotension were more frequently seen in patients on concomitant antihypertensive therapy. Some reactions were related to gastrointestinal reactions and associated volume loss.
Common (1% to 10%): Hypotension, orthostatic hypotension
Uncommon (0.1% to 1%): Syncope
Frequency not reported: Increased heart rate

Dermatologic

Common (1% to 10%): Hair loss
Very rarely (up to 1 in 10,000): non-arteritic anterior ischemic optic neuropathy (NAION)
Risk and side effect Mounjaro, ZepBound (tirzepatide): subcutaneous solution

Risk of Thyroid C-Cell TumorsIn both male and female rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether tirzepatide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide induced rodent thyroid C-cell tumors has not been determined. Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of tirzepatide and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with tirzepatide.

Cardiovascular

In pooled placebo-controlled trials, treatment with this drug resulted in a mean increase in heart rate of 2 to 4 beats per minute compared to a mean increase of 1 beat per minute in placebo-treated patients. Episodes of sinus tachycardia (associated with a concomitant increase from baseline in heart rate of at least 15 beats per minute) were reported in 4.6%, 5.9%, and 10% of patients treated with 5 mg, 10 mg, and 15 mg, respectively, compared to 4.3% treated with placebo; for patients enrolled in Japan, these episodes were reported in 7.1% (3/42), 9.3% (4/43), and 23% (10/43) of patients treated with 5 mg, 10 mg, and 15 mg, respectively, compared to 7% (3/43) treated with placebo. The clinical relevance of increased heart rate was uncertain.[Ref]

Very common (10% or more): Sinus tachycardia (up to 23%)
Frequency not reported: Increased heart rate[Ref]

Gastrointestinal

In pooled placebo-controlled trials, treatment with this drug resulted in mean increases from baseline in serum pancreatic amylase levels of 33% to 38% and serum lipase levels of 31% to 42%; placebo-treated patients had a mean increase from baseline in pancreatic amylase of 4% and no changes were observed in lipase. The clinical significance of elevations in lipase or amylase with this drug was unknown without other signs/symptoms of pancreatitis.[Ref]

Very common (10% or more): Nausea (up to 18%), diarrhea (up to 17%)
Common (1% to 10%): Vomiting, constipation, dyspepsia, abdominal pain, eructation, flatulence, gastroesophageal reflux disease, abdominal distension
Frequency not reported: Acute pancreatitis, increased serum pancreatic amylase levels, increased serum lipase levels[Ref]

Hepatic

Uncommon (0.1% to 1%): Acute gallbladder disease (cholelithiasis, biliary colic, cholecystectomy)[Ref]

Hypersensitivity

Common (1% to 10%): Hypersensitivity reactions (e.g., urticaria, eczema)[Ref]

Immunologic

Very common (10% or more): Anti-drug antibodies (up to 51%)
Common (1% to 10%): Neutralizing antibodies[Ref]

Local

Common (1% to 10%): Injection site reactions[Ref]

Metabolic

Very common (10% or more): Hypoglycemia (up to 19%), decreased appetite (up to 11%)[Ref]

Hypoglycemia was more frequent when this drug was used in combination with a sulfonylurea. In a clinical trial up to 104 weeks of therapy, when administered with a sulfonylurea, hypoglycemia (glucose level less than 54 mg/dL) occurred in 13.8%, 9.9%, and 12.8%, and severe hypoglycemia occurred in 0.5%, 0%, and 0.6% of patients treated with 5 mg, 10 mg, and 15 mg, respectively.