THE FDA HAS APPROVED THIS GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST AS AN ADJUNCT TO DIET AND EXERCISE TO IMPROVE GLYCEMIC CONTROL IN ADULTS WITH TYPE 2 DIABETES MELLITUS

Ozempic can cause:

+ Pancreatitis (persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting)
+ Diabetic Retinopathy Complications
+ Acute Kidney Injury/Renal Failure (nausea, vomiting, diarrhea, or dehydration) with possibility of dialysis as a medical intervention if renal failure occurs
+ Hypersensitivity Reactions (anaphylaxis, angioedema/swelling)
+ Macrovascular outcomes
+ Abdominal pain
+ Constipation
+ Changes in vision
+ Hypoglycemia (low blood sugar): dizziness/light-headedness, blurred vision, anxiety, irritability, or mood changes, sweating, slurred speech, hunger, confusion or drowsiness, shakiness, weakness, headache, fast heartbeat, or feeling jittery
+ Nausea
+ Vomiting
+ Diarrhea

SOURCES FROM THE FDA + NOVO NORDISK INC.

WARNING: RISK OF THYROID C-CELL TUMORS
See full prescribing information for complete boxed warning.

- **In rodents, semaglutide causes thyroid C-cell tumors. It is unknown whether OZEMPIC 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 (5.1, 13.1).**
- **OZEMPIC 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 (4, 5.1).**

HOW DOES IT WORK?

per the manufacturer:

What are the ingredients in OZEMPIC?
Active Ingredient: semaglutide
Inactive Ingredients: disodium phosphate dihydrate, propylene glycol, phenol and water for injection

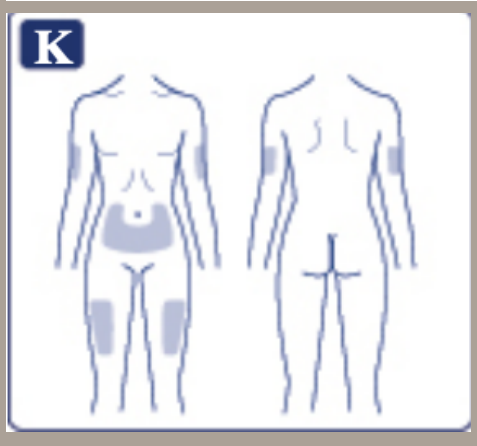
Semaglutide reduces blood glucose through a mechanism where it stimulates insulin secretion and lowers glucagon secretion, both in a glucose-dependent manner. Thus, when blood glucose is high, insulin secretion is stimulated and glucagon secretion is inhibited. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase.

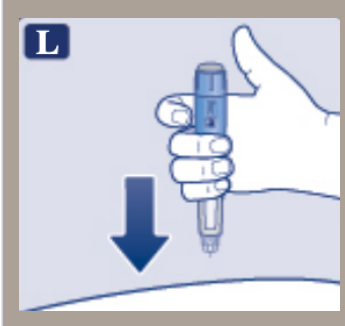
Semaglutide lowers fasting and postprandial blood glucose and reduces body weight. All pharmacodynamic evaluations were performed after 12 weeks of treatment (including dose escalation) at steady state with semaglutide 1 mg.

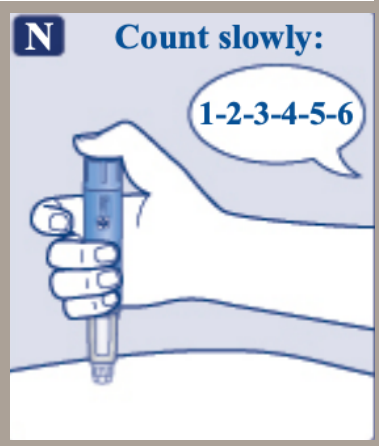
FDA U.S. FOOD & DRUG ADMINISTRATION

https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trial-snapshot-ozempic

OZEMPIC is a drug that improves blood sugar control in adults with type 2 diabetes mellitus (DM) when used in addition to diet and exercise.







OFF LABEL USE FOR WEIGHT-LOSS

according to Forbes,

Ozempic is a once-weekly injectable medication formulated to help adults with type 2 diabetes manage their blood sugar. Although not officially a weight loss drug, research suggests that people who take Ozempic may lose modest amounts of weight while on the medication. In fact, the active ingredient in Ozempic, known as semaglutide, is FDA-approved at higher doses for treating individuals living with obesity and other weight related medical problems under the name Wegovy.

Due to a Wegovy shortage coupled with Ozempic's weight loss effects going viral on social media, people without type 2 diabetes have begun using Ozempic off-label for weight loss.

https://www.forbes.com/health/body/ozempic-for-weight-loss/

Let's look at the manufacturer insert for Wegovy.

Thyroid C-cell Tumors: See Boxed Warning (5.1).
Acute Pancreatitis: Has occurred in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
Acute Gallbladder Disease: Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow-up are indicated (5.3).
Hypoglycemia: Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing the dose of insulin secretagogue or insulin may be necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia (5.4, 7.1).
Acute Kidney Injury: Has occurred. Monitor renal function when initiating or escalating doses of WEGOVY in patients reporting severe adverse gastrointestinal reactions or in those with renal impairment reporting severe adverse gastrointestinal reactions (5.5).

Hypersensitivity: Anaphylactic reactions and angioedema have been reported postmarketing. Discontinue WEGOVY if suspected and promptly seek medical advice (5.6).
Diabetic Retinopathy Complications in Patients with Type 2 Diabetes: Has been reported in trials with semaglutide. Patients with a history of diabetic retinopathy should be monitored (5.7).
Heart Rate Increase: Monitor heart rate at regular intervals (5.8).
Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue WEGOVY if symptoms develop (5.9).

The most common adverse reactions, reported in greater than or equal to 5% of patients treated with WEGOVY are: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, and gastroesophageal reflux disease (6.1).

Gastrointestinal Disorders: acute pancreatitis and necrotizing pancreatitis, sometimes resulting in death

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf

THYROID C-CELL TUMORS

per the ozempic manufacturer:

In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures *[see Nonclinical Toxicology (13.1)]*. It is unknown whether OZEMPIC causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

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

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values >50

ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

OZEMPIC is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of OZEMPIC and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

If you use GLP-1 receptor agonists, be aware of thyroid tumor symptoms: a mass in the neck, dysphagia (difficulty in swallowing), dyspnea (shortness of breath), or persistent hoarseness.

WHAT IS MEDULLARY THYROID CARCINOMA?

NIH NATIONAL CANCER INSTITUTE MyPART

Medullary thyroid cancer, or MTC, is a cancer that forms in the thyroid. The thyroid is a gland located in the front of your neck, just below the Adam's apple. It is responsible for sending out hormones to the rest of your body. The inside of the thyroid is called the medulla. The medulla contains special cells called parafollicular C cells that produce and release hormones. MTC happens when the C cells become cancerous and grow out of control. MTC may also be called medullary thyroid carcinoma.

MTC is usually treated by removing the thyroid.

Besides surgery, sometimes other treatments are also required, including radiation therapy or chemotherapy. Also, targeted therapies are available that act on changes in DNA found in some cases of MTC.

MTC can start as a lump in the throat. The tumor growing in the thyroid can make your voice hoarse by blocking your vocal chords or it can make it hard to breathe by blocking your windpipe. Sometimes people can have MTC for a long time without symptoms because the tumor remains small. MTC can spread to other organs, such as lung, liver, bones, and brain.

https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-endocrine-tumor/medullary-thyroid-cancer

PREGNANCY + BREASTFEEDING

per the manufacturer:

USE IN SPECIFIC POPULATIONS

Females and Males of Reproductive Potential: Discontinue OZEMPIC in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide (8.3).

There are limited data with semaglutide use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. There are clinical considerations regarding the risks of poorly controlled diabetes in pregnancy *(see Clinical Considerations)*. Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. OZEMPIC should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.1-, 0.4-, and 1.1-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at the human exposure.

There are no data on the presence of semaglutide in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats, however, due to species-specific differences in lactation physiology, the clinical relevance of these data are not clear *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OZEMPIC and any potential adverse effects on the breastfed infant from OZEMPIC or from the underlying maternal condition.

ADDITIONAL WARNINGS

per the manufacturer:

5.4 Never Share an OZEMPIC Pen Between Patients

OZEMPIC pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.

Inform patients of the potential risks and benefits of OZEMPIC and of alternative modes of therapy. Inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and A_{1c} testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications. Advise patients to seek medical advice promptly during periods of stress such as fever, trauma, infection, or surgery as medication requirements may change.

Instruct patients to reread the Medication Guide each time the prescription is renewed.

It is not known if OZEMPIC is safe and effective for use in children under 18 years of age.

Your dose of OZEMPIC and other diabetes medicines may need to change because of:

- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, fever, trauma, infection, surgery or because of other medicines you take.

6.2 Immunogenicity

Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with OZEMPIC may develop anti-semaglutide antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the incidence of antibodies to semaglutide in the studies described below cannot be directly compared with the incidence of antibodies in other studies or to other products.

FOR FURTHER RESEARCH

NIH National Library of Medicine
National Center for Biotechnology Information

Boosting GLP-1 by Natural Products

The prevalence of diabetes mellitus is growing rapidly. Diabetes is the underlying cause of many metabolic and tissue dysfunctions, and, therefore, many therapeutic agents have been developed to regulate the glycemic profile. Glucagon-like peptide-1 (GLP-1) receptor agonists are a newly developed class of antidiabetic drugs that have potent hypoglycemic effects via several molecular pathways. In addition to synthetic GLP-1 receptor agonists, some evidence suggests that natural products may have modulatory effects on GLP-1 expression and secretion. In the current study, we conclude that certain herbal-based constituents, such as berberine, tea, curcumin, cinnamon, wheat, soybean, resveratrol, and gardenia, can exert an influence on GLP-1 release.

https://pubmed.ncbi.nlm.nih.gov/34981502/