Semaglutide (OZEMPIC) Injection for Type 2 Diabetes Mellitus
Criteria for Use
April 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National Formulary Committee Monograph on this drug at the *PBM INTRAnet* site for further information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive Semaglutide.

- ☐ Personal or family history of medullary thyroid carcinoma or with Multiple Endocrine Neoplasia syndrome type 2 (contraindication/boxed warning against use)
- ☐ Severe gastrointestinal dysmotility including gastroparesis (unless risks/benefits are discussed with the patient and documented in the Federal EHR with a plan to monitor and follow GI symptoms)
- ☐ History of pancreatitis (does not pertain to patients for whom the cause of pancreatitis is known and no longer presents a risk)
- ☐ Pregnancy^1
- ☐ Known PDR, severe NPDR, clinically significant ME, or DME unless risks/benefits are discussed with the patient and documented in the Federal EHR with a plan to monitor and follow-up with an eye specialist who is informed upon initiation ^2
- ☐ Low body weight and/or presence of sarcopenia (unless risks/benefits are discussed with the patient and documented in the Federal EHR with a plan to closely monitor and follow changes in weight)
- ☐ Concomitant use of dipeptidyl peptidase 4 (DPP-4) inhibitors (e.g., sitagliptin, saxagliptin, linagliptin, etc.) (Additional benefit has not been shown with concomitant use with semaglutide or other GLP-1RA)

Abbreviations: DME=diabetic macular edema; EHR=electronic health record; GLP-1RA=glucagon-like peptide-1 receptor agonist; ME=macular edema; NPDR=nonproliferative diabetic retinopathy; PDR=proliferative diabetic retinopathy

1. **Insulin is generally the preferred treatment during pregnancy**. Discontinue semaglutide in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide. If semaglutide is being considered, use only if the potential benefit justifies the potential risk to the fetus and mother. Pregnancy and infant outcomes following exposure to semaglutide is ongoing via a registry; enrollment in the registry is recommended.
2. Diabetic retinopathy complications are recognized as a class effect. Differences in risk may be related to the rate and extent of glucose lowering. Before considering a GLP-1 agonist, the provider should have the results of diabetic eye examination completed within past 12 months on file. Patients with a history of diabetic retinopathy should have planned follow-up with the eye provider to monitor for progression. Ophthalmology consult should be obtained any time there are concerns related to use in patients with diabetic retinopathy.

Inclusion Criteria

The following criteria must be met.

- ☐ Diagnosis of Type 2 diabetes mellitus. (T2DM)

Additional Inclusion Criteria

ONE of the following criteria must be met:

- ☐ Patient has established ASCVD and/or CKD and is not a good candidate for empagliflozin. ^3-4

☐ Patient whose glycemic goals are not met with empagliflozin plus maximally tolerated doses of metformin, unless unable to use. ^3-8

☐ To replace selected drugs (insulin, sulfonylurea, DPP-4, TZD), irrespective of A1c, with intent to reduce weight, hypoglycemic risk or improve outcomes ^3-6

3. Semaglutide and empagliflozin reduce major adverse cardiovascular events (MACE), slow progression of CKD and lead to weight loss. Empagliflozin has beneficial effects in patients with heart failure (e.g., reduced hospitalization and CV death - HFrEF and HFpEF). Semaglutide improves symptoms in HFpEF and reduces stroke risk. *The improvement in outcomes was observed in patients with type 2 diabetes with mean baseline A1c >7%.* Although a combination of semaglutide + empagliflozin can lead to improved glycemic control, direct evidence from prospective, randomized controlled trials are lacking to confirm that the combination further reduces CV risk or further slows progression of CKD vs. use of either agent alone.
4. Risks with empagliflozin may include volume depletion, genitourinary tract infections, genital mycotic infections, ketoacidosis, etc. (refer to package labeling). Not recommended for glycemic control in patients with eGFR <30 mL/min/1.73 m^2. Additionally, not recommended for initiation to reduce CV or CKD risk in patients with eGFR <20 mL/min/1.73 m^2.
5. In patients (with or without known ASCVD and/or CKD) whose glycemic goals are not met on empagliflozin, metformin should be used prior to adding semaglutide or another GLP-1 agonist, unless unable to use.
6. Metformin is contraindicated in patients with eGFR <30 mL/minute/1.73 m^2. Although initial therapy with metformin in patients with T2DM and ASCVD or CKD is no longer recommended (prior to a SGLT-2 **or** GLP-1), it has a high probability of achieving glycemic goals with a neutral effect on weight and potential benefit in reducing MACE. Therefore, in patients taking empagliflozin who do not meet their glycemic goals, metformin should be added to empagliflozin prior to adding semaglutide. The gastrointestinal (GI) tolerability of metformin may be improved by starting with lower doses and titrating slowly, taking with food, and using the sustained-action (SA) formulation.
7. Insulin may be considered at any time prior to using a GLP-1 agonist; however, insulin is preferred if patient is symptomatic, has blood sugars $\geq$ 300 mg, A1c is >10% or the desired A1C reduction is beyond what is achievable by a GLP-1 agonist. In clinical trials the mean reduction in A1c when semaglutide is added to oral hypoglycemic agents ranges from 1.3% to 1.5%. The mean reduction in A1c when semaglutide was used with basal insulin was 1.3% (0.5mg) and 1.7% (1.0mg).
8. Refer to the VA/DoD Type 2 Diabetes Guidelines for recommendations on individualizing A1c targets. Use the URL to access guidelines. https://www.healthquality.va.gov/guidelines/CD/diabetes/

Additional information:

- Atherosclerotic Cardiovascular Disease (ASCVD): history of acute coronary syndrome or myocardial infarction, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or atherosclerotic peripheral artery disease.
- Heart failure with reduced ejection fraction (HFrEF) or with preserved ejection fraction (HFpEF)
- Thiazolidinedione (TZD), (e.g., pioglitazone)
- Chronic Kidney Disease (CKD): eGFR <60mL/min/1.73m^2 OR Urinary Albumin-to-Creatinine Ratio >= 30mg/g
- GLP-1 receptor agonists in combination with alpha glucosidase inhibitors or meglitinides are not recommended due to lack of or insufficient data regarding their combined use.

NOTE: Oral semaglutide (nonformulary) should be reserved for patients physically unable to use injectable therapy (e.g., dexterity or vision limitations, etc.).

Supplemental Information

- Type 1 Diabetes-Semaglutide (OZEMPIC) is not FDA approved for use in Type 1 diabetics for glycemic control. However, small, retrospective studies have shown improvements in body weight and glycemic measures with addition of semaglutide to insulin. There are several ongoing studies of semaglutide added to insulin in type 1 diabetics investigating improvements in weight and secondarily, glycemic stability and control that may help guide appropriate, safe, and effective use in this population. In a systematic review and meta-analysis, the efficacy and safety of GLP-1 receptor agonists (RA) or SGLT2 inhibitors added to insulin in patients with type 1 diabetes was investigated. Addition of GLP-1 RA lowered A1c (0.56%), increased time in range and reduced body weight, BMI and total and basal daily insulin requirements.[1] The authors recommend that these findings be confirmed in a large, longer-term trial to help identify the optimal candidate for GLP-1 RA therapy and their role in routine care. **Please refer to the weight management criteria for use documents for guidance on patient selection in this population.**
- Metabolic dysfunction-associated steatotic liver disease (MASLD) refers to liver steatosis in patients with at least one metabolic risk factor including obesity, type 2 diabetes, hypertension, and dyslipidemia. Patients with MASLD have fat accumulation in the liver generally exceeding 5%, have no other cause for liver steatosis and consume little to no alcohol. Obesity is thought to be the most common cause of MASLD. MASLD can progress to metabolic-associated steatotic hepatitis (MASH) in a proportion of those with MASLD, especially in patients with >1 metabolic risk factor. However, the cause(s) for MASH to develop is unclear. MASLD can be reversible with weight loss, avoidance of alcohol and ensuring concomitant metabolic risk factors are properly addressed and managed (e.g., type 2 diabetes, hyperlipidemia, and hypertension). **Please refer to the weight management and MASH criteria for use documents for guidance on patient selection.**
- Risk factors for pancreatitis may include hypertriglyceridemia (e.g., >1000 mg/dL, gallstones with intact gallbladder, alcohol use disorder and/or excessive use of alcohol, etc.)
- There are no data on the presence of semaglutide in human milk, the effects on the breastfed infant, or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for semaglutide and potential adverse effects on the breastfed infant or from the underlying maternal condition.

Abdel-Rahman SM, Al-Shiab R, Shah E, et al. Efficacy and Safety of GLP-1 Receptor Agonists and SGLT2 Inhibitors as Adjuncts to Insulin in Type 1 Diabetes: Systematic Review and Meta-Analysis.

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