Semaglutide (OZEMPIC) Injection
Criteria for Use
July 2022

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

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 UTILIZE 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.**

Exclusion Criteria

- ☐ Type 1 diabetes
- ☐ Personal or family history of medullary thyroid carcinoma or with Multiple Endocrine Neoplasia syndrome type 2
- ☐ Severe gastrointestinal dysmotility including gastroparesis
- ☐ 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 have been discussed with the patient and is documented in the EHR along with monitoring plans and follow-up with an eye specialist who is informed at the time of initiation ^2

Relative Exclusions

- ☐ Risk factors for pancreatitis (e.g., untreated fasting triglyceride level > 1000mg/dL, known gallstones with intact gallbladder, alcohol use disorder)

Abbreviations: DME=diabetic macular edema; EHR=electronic health record; 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 suspected 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

Patients WITH Atherosclerotic Cardiovascular Disease and/or Chronic Kidney Disease^1

- ☐ Type 2 diabetes **AND** receiving metformin unless unable to use metformin
- ☐ Not a good candidate for empagliflozin^2

AND at least ONE of the following:

☐ Established atherosclerotic cardiovascular disease
☐ eGFR <60mL/min/1.73m^2 OR Urinary Albumin-to-Creatinine Ratio >= 30mg/g

1. **Atherosclerotic Cardiovascular Disease:** history of acute coronary syndrome or myocardial infarction, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

2. Risks for empagliflozin may include volume depletion, genitourinary tract infections, and ketoacidosis (refer to package labeling)

Patients with Type 2 Diabetes WITHOUT Atherosclerotic Cardiovascular Disease and/or Chronic Kidney Disease

Select ONE of the following:

☐ Inadequate glycemic control on two or more oral medications, one of which should be metformin, unless unable to use ^3-5
☐ Inadequate glycemic control on basal insulin, titrated as feasible, to an acceptable fasting blood glucose level, plus one or more oral medications, one of which should be metformin, unless unable to use^6-7

Reserve oral semaglutide (nonformulary) for those unable to use injectable therapy (e.g., dexterity or vision limitations, etc.). Consider other oral formulary agents before using oral semaglutide.

3. For patients with BMI greater or equal to 27kg/m^2, empagliflozin is recommended as the second oral agent (to metformin), unless unable to use

4. Refer to the VA/DoD Diabetes Guidelines https://www.healthquality.va.gov/ for recommendations on individualizing A1C targets

5. GLP-1 agonists in combination with alpha glucosidase inhibitors, meglitinides or DPP-4 inhibitors are not recommended due to lack of or insufficient data regarding their combined use.

6. Insulin may be considered at any time prior to using a GLP-1 agonist; however, insulin is preferred if patient is symptomatic 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).

7. The data for GLP-1 agonists in combination with both basal and prandial insulin or with U500 insulin are very limited at present. Concomitant use of GLP-1 agonists with regimens containing basal insulin AND prandial insulin (including premixed formulations) or with U500 may be done on a case-by-case basis in consultation with an endocrinologist or diabetes specialist.

Other Justification:

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November 2020 replaces GLP1 Agonist CFU; (rev July 2021; rev April 2022, July 2022)
Updated versions may be found at *PBM INTERnet* or *PBM INTRAnet*