Ozempic® (semaglutide) – New indication; Rybelsus® (semaglutide) – Label update

- On January 16, 2020, Novo Nordisk announced the FDA approval of Ozempic (semaglutide) injection, to reduce the risk of major adverse cardiovascular events (MACE) (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus (T2DM) and established cardiovascular (CV) disease.
    - Ozempic has not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.
    - Ozempic is not a substitute for insulin. Ozempic is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.
- Ozempic is also approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
- The approval of Ozempic for the new indication was based on SUSTAIN 6, a placebo-controlled, double-blind, cardiovascular outcomes study in 3,297 patients with inadequately controlled T2DM and atherosclerotic CV disease. Patients were randomized to Ozempic (0.5 mg or 1 mg) once weekly or placebo for a minimum observation time of 2 years. The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included CV death, non-fatal myocardial infarction and non-fatal stroke.
    - Ozempic significantly reduced the occurrence of MACE. The estimated hazard ratio (HR) for time to first MACE was 0.74 (95% CI: 0.58, 0.95).
- In addition, the label for oral semaglutide (Rybelsus®) was updated to include clinical data from PIONEER 6, a placebo-controlled, double-blind study in 3,183 patients with inadequately controlled T2DM and atherosclerotic CV disease. Patients were randomized to Rybelsus 14 mg once daily or placebo for a median observation time of 16 months. The same three-part MACE outcome was used as the primary endpoint.
    - Rybelsus demonstrated non-inferiority to placebo (HR 0.79, 95% CI: 0.57, 1.11) over the median observation time of 16-months.
- In June 2019, Novo Nordisk initiated the SOUL CVOT in 9,642 adults with T2DM and established CV disease to further evaluate the CV effect of Rybelsus.
- Ozempic and Rybelsus carry a boxed warning for risk of thyroid C-cell tumors.
- The recommended starting dose of Ozempic for all T2DM patients is 0.25 mg subcutaneously once weekly for 4 weeks. The 0.25 mg dose is intended for treatment initiation and is not effective for glycemic control. After 4 weeks on the 0.25 mg dose, the dosage should be increased to 0.5 mg once weekly.
    - If additional glycemic control is needed after at least 4 weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly. The maximum recommended dosage is 1 mg once weekly.
- The recommended starting dose of Rybelsus for all T2DM patients is 3 mg once daily for 30 days. The 3 mg dose is intended for treatment initiation and is not effective for glycemic control. After 30 days on the 3 mg dose, the dose should be increased to 7 mg once daily.

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- The dose may be increased to 14 mg once daily if additional glycemic control is needed after at least 30 days on the 7 mg dose.