CLINICAL UPDATE

Brand Name	Ozempic®
Generic Name	semaglutide
Drug Manufacturer	Novo Nordisk

Clinical Update

TYPE OF CLINICAL UPDATE

New strength

FDA APPROVAL DATE

January 16, 2020

LAUNCH DATE

N/A

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Efficacy-New Indication

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Ozempic® is a glucagon-like peptide 1 (GLP-1) receptor agonist indicated as:

- An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease

MECHANISMS OF ACTION

Semaglutide is selective glucagon-like peptide-1 (GLP-1) receptor agonist. Acting on the same receptor as the endogenous hormone incretin, semaglutide increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, and slows gastric emptying. Increases first- and second-phase insulin secretion.

DOSAGE FORM(S) AND STRENGTH(S)

- Injection: 2 mg/1.5 mL (1.34 mg/mL) available in:
  - Single-patient-use pen that delivers 0.25 mg or 0.5 mg per injection.
  - Single-patient-use pen that delivers 1 mg per injection.
- Injection: 4 mg/3 mL (1.34 mg/mL) available in:
  - Single-patient-use pen that delivers 1 mg per injection

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DOSE & ADMINISTRATION

- Start at 0.25 mg once weekly. After 4 weeks, increase the dose to 0.5 mg once weekly. If after at least 4 weeks additional glycemic control is needed, increase to 1 mg once weekly.
- Administer once weekly at any time of day, with or without meals.
- If a dose is missed administer within 5 days of missed dose.
- Inject subcutaneously in the abdomen, thigh, or upper arm

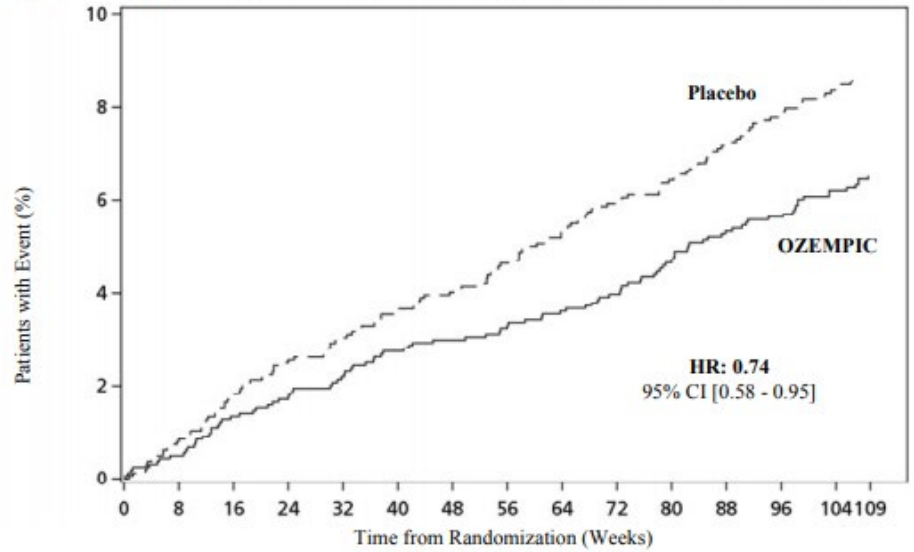
EFFICACY

The efficacy is based on the results from the SUSTAIN 6 cardiovascular outcomes trial (CVOT) which examined the cardiovascular safety of adding Ozempic® or placebo to standard of care in adults with type 2 diabetes and established cardiovascular disease. In the 2-year SUSTAIN 6 trial, Ozempic® significantly reduced the risk of the occurrence of a three-component Major Adverse Cardiovascular Event (MACE) endpoint consisting of cardiovascular death, non-fatal heart attack or non-fatal stroke. The estimated relative risk reduction of Major Adverse Cardiovascular Event (MACE) was 26% vs placebo (HR 0.74 [95% CI: 0.58, 0.95], p<0.001 for noninferiority, median observation time 2.1 years) with the primary composite outcome occurring in 6.6% of patients treated with Ozempic® vs 8.9% with placebo. During the trial, gastrointestinal adverse events were more frequent in the Ozempic® group than in the placebo group. The majority of gastrointestinal adverse events occurred during the first 30 weeks.

In the SUSTAIN-6 cardiovascular event reduction study of Ozempic® versus placebo, the drug cut the risk of cardiovascular events by 26%, stroke risks by 39% and heart attack by 26%, though the latter was not statistically significant.

For the primary analysis, a Cox proportional hazards model was used to test for non-inferiority of Ozempic® to placebo for time to first MACE using a risk margin of 1.3. The statistical analysis plan pre specified that the 0.5 mg and 1 mg doses would be combined. Type-1 error was controlled across multiple tests using a hierarchical testing strategy. Ozempic® significantly reduced the occurrence of MACE. The estimated hazard ratio for time to first MACE was 0.74 (95% CI: 0.58, 0.95). Refer to Figure 6 and Table 8.

Figure 6. Kaplan-Meier: Time to First Occurrence of a MACE in the SUSTAIN 6 Trial



Patients at risk

OZEMPIC	1648	1619	1601	1584	1568	1543	1524	1505
Placebo	1649	1616	1586	1567	1534	1508	1479	1460

Table 8. Treatment Effect for MACE and its Components, Median Study Observation Time of 2.1 Years

	Placebo N=1649 (%)	OZEMPIC N=1648 (%)	Hazard ratio vs Placebo (95% CI)[a]
Composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke (time to first occurrence)	146 (8.9)	108 (6.6)	0.74 (0.58, 0.95)
Non-fatal Myocardial Infarction	64 (3.9)	47 (2.9)	0.74 (0.51, 1.08)
Non-fatal Stroke	44 (2.7)	27 (1.6)	0.61 (0.38, 0.99)
Cardiovascular Death	46 (2.8)	44 (2.7)	0.98 (0.65, 1.48)
Fatal or Non-fatal Myocardial Infarction	67 (4.1)	54 (3.3)	0.81 (0.57, 1.16)
Fatal or Non-fatal Stroke	46 (2.8)	30 (1.8)	0.65 (0.41, 1.03)