AUSTRALIAN PRODUCT INFORMATION

OZEMPIC®

(semaglutide) solution for injection

1. NAME OF THE MEDICINE

semaglutide (rys)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ozempic 0.25 mg, 0.5 mg/dose

One mL of solution contains 1.34 mg of semaglutide. One pre-filled pen contains 2 mg semaglutide in 1.5 mL solution.

Ozempic 1 mg/dose

One mL of solution contains 1.34 mg semaglutide. One pre-filled pen contains 4 mg semaglutide in 3 mL solution.

Semaglutide is a human glucagon-like-peptide-1 (GLP-1) receptor agonist produced in *Saccharomyces cerevisiae* by recombinant DNA technology followed by protein purification.

For the full list of excipients, see Section 6.1 List of Excipients.

3. PHARMACEUTICAL FORM

Ozempic solution for injection is provided in a pre-filled multidose disposable pen, which contains semaglutide in a 1.5 mL or 3 mL cartridge.

It is a clear and colourless, or almost colourless, isotonic solution with pH = 7.4.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ozempic is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is not tolerated or contraindicated.
- in addition to other medicinal products for the treatment of type 2 diabetes.

4.2 Dose and Method of Administration

Dosage

Ozempic starting dose is 0.25 mg once weekly. After 4 weeks, the dose should be increased to 0.5 mg once weekly. After at least 4 weeks with a dose of 0.5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control.

Ozempic 0.25 mg is not a maintenance dose.

When Ozempic is added to existing metformin and/or thiazolidinedione therapy, the current dose of metformin and/or thiazolidinedione can be continued unchanged.

When Ozempic is added to existing therapy of a sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia (see section 4.4 Special Warnings and Precautions for Use).

The use of Ozempic does not require blood glucose self-monitoring. Self-monitoring may be performed when Ozempic is used together with sulfonylurea or insulin in order to allow adjustment of the dose of these medications.

Method of Administration

Ozempic is to be administered once weekly, on the same day each week, at any time of the day, with or without meals.

Ozempic is to be injected subcutaneously in the abdomen, in the thigh or in the upper arm. The injection site can be changed without dose adjustment. Ozempic should not be administered intravenously or intramuscularly. For further information on administration, see section 6 Pharmaceutical Particulars.

The day of weekly administration can be changed if necessary as long as the time between two doses is at least 3 days (>72 hours). After selecting a new dosing day, once-weekly dosing should be continued.

If a dose is missed, it should be administered as soon as possible and within 5 days after the missed dose. If more than 5 days have passed, the missed dose should be skipped, and the next dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

Dosage Adjustment

Elderly (≥65 years old)

No dose adjustment is required based on age. Therapeutic experience in patients ≥75 years of age is limited (see section 5.2 Pharmacokinetic Properties).

Gender

No dose adjustment is required based on gender.

Race and Ethnicity

No dose adjustment is required based on race and ethnicity.

Patients with hepatic impairment

No dose adjustment is required for patients with hepatic impairment (see section 5.2 Pharmacokinetic Properties). Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.

Patients with renal impairment

No dose adjustment is required for patients with renal impairment. Experience with the use of semaglutide in patients with severe (CrCL <30 mL/min) renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease (see section 5.2 Pharmacokinetic Properties).

Children and adolescents

Safety and efficacy of Ozempic in children and adolescents below 18 years have not been studied.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 List of Excipients.

4.4 Special Warnings and Precautions for Use

Ozempic should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Ozempic is not a substitute for insulin.

Gastrointestinal Effects

Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions. This should be considered when treating patients with impaired renal function as nausea, vomiting, and diarrhoea, may cause dehydration which could cause a deterioration of renal function.

Acute Pancreatitis

Acute pancreatitis has been observed with the use of GLP-1 receptor agonists. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Ozempic should be discontinued; if confirmed, Ozempic should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Hypoglycaemia

Patients treated with Ozempic in combination with a sulfonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with Ozempic.

Diabetic Retinopathy

In patients with diabetic retinopathy treated with insulin and semaglutide, an increased risk of developing diabetic retinopathy complications has been observed (see section 4.8 Adverse Effects (Undesirable Effects)). Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy.

Long-term glycaemic control decreases the risk of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for worsening and treated according to clinical guidelines.

Heart Failure

There is no therapeutic experience in patients with congestive heart failure New York Heart Association (NYHA) class IV and therefore use of semaglutide is not recommended in these patients.

Use in hepatic impairment

Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.

Use in renal impairment

Experience with the use of semaglutide in patients with severe (CrCL < 30 mL/min) renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease (see sections 5.1 Pharmacodynamic Properties and 5.2 Pharmacokinetic Properties).

Use in elderly

See section 5.2 Pharmacokinetic Properties.

Paediatric Use

The safety and efficacy of semaglutide in children and adolescents aged below 18 years has not been studied.

Effects on laboratory tests

No data available.

4.5 Interactions with Other Medicines and Other Forms of Interactions

In vitro studies have shown very low potential for semaglutide to inhibit or induce CYP enzymes, and to inhibit drug transporters.

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral medicinal products, therefore semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption. The potential effect of semaglutide on the absorption of co-administered oral medications was studied in trials at semaglutide 1 mg steady state exposure.

No clinically relevant drug–drug interaction with semaglutide (Figure 1) was observed based on the evaluated medications. Therefore, no dose adjustment is required when co-administered with semaglutide.

Oral Contraceptives

Semaglutide is not anticipated to decrease the effectiveness of oral contraceptives as semaglutide did not change the overall exposure of ethinylestradiol and levonorgestrel to a clinically relevant degree when an oral contraceptive combination medicinal product (0.03 mg ethinylestradiol/0.15 mg levonorgestrel) was co-administered with semaglutide. Exposure of ethinylestradiol was not affected; an increase of 20% was observed for levonorgestrel exposure at steady state. C_{max} was not affected for any of the compounds.

Atorvastatin

Semaglutide did not change the overall exposure of atorvastatin following a single dose administration of atorvastatin (40 mg). Atorvastatin C_{max} was decreased by 38%. This was assessed not to be clinically relevant.

Digoxin

Semaglutide did not change the overall exposure or C_{max} of digoxin following a single dose of digoxin (0.5 mg).

Metformin

Semaglutide did not change the overall exposure or C_{max} of metformin following dosing of 500 mg twice daily over 3.5 days.

Warfarin

Semaglutide did not change overall exposure or C_{max} of R- and S-warfarin following a single dose of warfarin (25 mg), and the pharmacodynamic effects of warfarin as measured by the international normalised ratio were not affected in a clinically relevant manner.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility

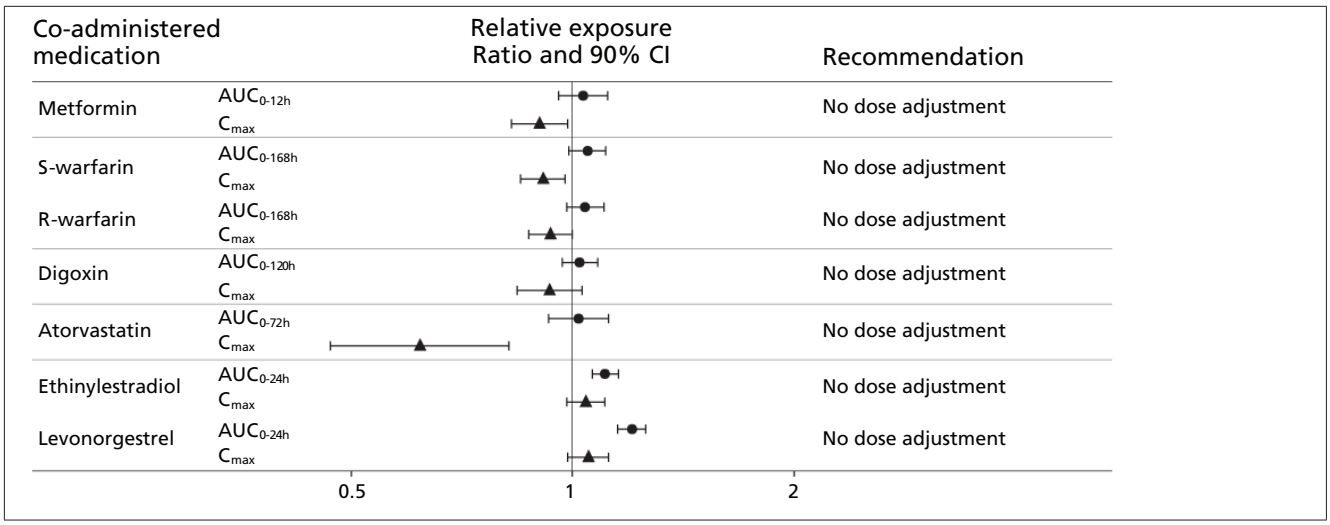
The effect of semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats at daily SC doses of 828 µg/kg, resulting in exposures approximately 13 times the clinical AUC. In female rats, an increase in oestrous length and a small reduction in number of ovulations were observed at doses associated with maternal body weight loss (≥ 30 µg/kg/day SC, resulting in subclinical exposures).

Use in pregnancy

Pregnancy Category: D

Semaglutide should not be used during pregnancy. Women of childbearing potential are recommended to use contraception when treated with semaglutide. If a patient wishes to become pregnant, or pregnancy occurs, semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life (see section 5.1 Pharmacodynamic Properties).

Studies in animals have shown reproductive toxicity when semaglutide was administered during organogenesis. In pregnant rats, embryofetal toxicity (lethality, impaired growth and an increased incidence of fetal abnormalities) was observed at subclinical plasma exposures. Mechanistic



Relative exposure in terms of AUC and C_{max} for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinylestradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), digoxin and atorvastatin were assessed after a single dose.
Abbreviations: AUC: area under the curve. C_{max}: maximum concentration. CI: confidence interval.

Figure 1: Impact of semaglutide on the exposure of co-administered oral medications

studies suggest a direct GLP-1 receptor mediated role of semaglutide on some of the effects in rats (species specific). In pregnant rabbits, pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternebra) fetal abnormalities were observed at ≥0.0025 mg/kg/day, at clinically relevant exposures. In pregnant cynomolgus monkeys, pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) and with an increase in early pregnancy losses at ≥0.075 mg/kg twice weekly (>2.7 fold clinical exposure at 1 mg/week). Exposures at the NOAEL in all species were subclinical and a direct effect of semaglutide on the fetus cannot be excluded.

Use in lactation

In lactating rats, semaglutide was excreted in milk. A risk to a breast-fed child cannot be excluded. Semaglutide should not be used during breast-feeding.

4.7 Effects on Ability to Drive and Use Machines

Ozempic has no or negligible influence on the ability to drive or use machines. When it is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.

Adverse effects of Ozempic include dizziness which could affect the ability to drive or use machines (see Section 4.8 Adverse Effects (Undesirable Effects)).

4.8 Adverse Effects (Undesirable Effects)

Summary of the Safety Profile

In 8 phase 3a trials, 4,792 patients were exposed to Ozempic alone or in combination with other glucose lowering medicinal products. The duration of the treatment ranged from 30 weeks to 2 years.

The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea, diarrhoea and vomiting. In general, these reactions were mild or moderate in severity and of short duration.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

Tabulated List of Adverse Events

Table 1: Treatment-emergent adverse events with frequency ≥5% comparing Ozempic 0.5 mg dose, Ozempic 1.0 mg dose with comparators

Adverse Event Term	Ozempic 0.5 mg dose % (n=1373)	Ozempic 1.0 mg dose % (n=1777)	Comparator % (n=1657)
Nausea	17.0	19.9	6.3
Vomiting	6.4	8.4	3.3
Dyspepsia	4.1	5.2	2.1
Diarrhoea	12.2	13.3	5.7
Constipation	6.9	6.2	2.7
Nasopharyngitis	14.5	10.7	13.8
Lipase increased	8.7	8.5	6.3
Headache	5.3	6.4	5.5
Decreased appetite	6.3	7.2	2.0

Adverse Reactions

Table 2 lists adverse reactions identified in phase 3a trials in patients with type 2 diabetes (further described in section 5.1 Pharmacodynamic Properties). The frequencies of the adverse reactions are based on a pool of the phase 3a trials excluding the cardiovascular outcomes trial.

The reactions are listed below by system organ class and absolute frequency. Frequencies are defined as: very common: (≥1/10); common: (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare: (≥1/10,000 to <1/1,000); and very rare: (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse reactions from controlled phase 3a trials

MedDRA system organ class	Very common	Common	Uncommon	Rare
Immune-system disorders			Hypersensitivity[c]	Anaphylactic reaction
Metabolism and nutrition disorders	Hypoglycaemia[a] when used with insulin or sulfonylurea	Hypoglycaemia[a] when used with other OADs Decreased appetite		
Nervous system disorders		Dizziness	Dysgeusia	
Eye disorders		Diabetic retinopathy complications[b]		
Cardiac disorders			Increased heart rate	
Gastrointestinal disorders	Nausea Diarrhoea	Vomiting Abdominal pain Abdominal distension Constipation Dyspepsia Gastritis Gastro-oesophageal reflux disease Eructation Flatulence	Acute pancreatitis	
Hepatobiliary disorders		Cholelithiasis		
General disorders and administration site conditions		Fatigue	Injection site reactions	
Investigations		Increased lipase Increased amylase Weight decreased		

[a] Hypoglycaemia defined as severe (requiring the assistance of another person) or symptomatic in combination with a blood glucose <3.1 mmol/L.
[b] Diabetic retinopathy complications is a composite of: need for retinal photocoagulation, need for treatment with intravitreal agents, vitreous haemorrhage, onset of diabetes-related blindness. Frequency based on cardiovascular outcomes trial.
[c] Grouped term covering also adverse events related to hypersensitivity such as rash and urticaria.

2-year cardiovascular outcomes and safety trial

In a high cardiovascular risk population, the adverse reaction profile was similar to that seen in the other phase 3a trials (described in section 5.1 Pharmacokinetic Properties).

Description of Selected Adverse Reactions

Hypoglycaemia

No episodes of severe hypoglycaemia were observed when Ozempic was used as monotherapy. Severe hypoglycaemia was primarily observed when Ozempic was used with a sulfonylurea (1.2% of subjects, 0.03 events/patient year) or insulin (1.5% of subjects, 0.02 events/patient year). Few severe episodes (0.1% of subjects, 0.001 events/patient year) were observed with Ozempic in combination with oral antidiabetics other than sulfonylureas.

Gastrointestinal Adverse Reactions

Nausea occurred in 17.0% and 19.9% patients when treated with Ozempic 0.5 mg and 1 mg respectively, diarrhoea in 12.2% and 13.3% and vomiting in 6.4% and 8.4%. Most events were mild to moderate in severity and of short duration. The events led to treatment discontinuation in 3.9% and 5.9% of subjects. The events were most frequently reported during the first months on treatment. Patients with low body weight may experience more gastrointestinal side effects when treated with semaglutide.

Diabetic Retinopathy Complications

In a 2-year clinical trial involving 3,297 patients with type 2 diabetes and high cardiovascular risk, long duration of diabetes and poorly controlled

blood glucose, adjudicated events of diabetic retinopathy complications occurred in more patients treated with Ozempic (3.0%) compared to placebo (1.8%). The treatment difference appeared early and persisted throughout the trial. The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy treated with insulin at baseline. In the patients that did not have a documented history of diabetic retinopathy the number of events were similar for Ozempic and placebo.

In other clinical trials up to 1 year involving 4,807 patients with type 2 diabetes patients, adverse events related to diabetic retinopathy were reported in similar proportions of subjects treated with Ozempic (1.7%) and comparators (2.0%).

Discontinuation Due to an Adverse Event

The incidence of discontinuation of treatment due to adverse events was 6.1% and 8.7% for patients treated with semaglutide 0.5 mg and 1 mg respectively, versus 1.5% for placebo. The most frequent adverse events leading to discontinuation were gastrointestinal.

Injection Site Reactions

Injection site reactions (e.g. injection site rash, erythema) have been reported by 0.6% and 0.5% of patients receiving semaglutide 0.5 mg and 1 mg respectively. A similar rate of injection site reactions was experienced by patients receiving placebo. These reactions have usually been mild.

Immunogenicity

Consistent with the potentially immunogenic properties of medicinal products containing proteins or peptides, patients may develop antibodies following treatment with semaglutide. The proportion of patients tested positive for anti-semaglutide antibodies at any time point post-baseline was low (1–2%) and no patients had anti-semaglutide neutralising antibodies or anti-semaglutide antibodies with endogenous GLP-1 neutralising effect at end-of-trial.

Heart Rate Increase

Increased heart rate has been observed with GLP-1 receptor agonists. In the phase 3a trials, mean increases of 1 to 6 beats per minute (bpm) from a baseline of 72 to 76 bpm were observed in subjects treated with semaglutide. In a long-term trial in subjects with cardiovascular risk factors, 16% of semaglutide-treated subjects had an increase in heart rate of >10 bpm compared to 11% of subjects on placebo after 2 years of treatment.

Increases in Amylase and Lipase

In placebo-controlled trials, patients exposed to semaglutide had a mean increase from baseline in amylase of 13% and lipase of 22%. These changes were not observed in placebo-treated patients. In the absence of other signs and symptoms of acute pancreatitis, elevations in pancreatic enzymes alone are not predictive of acute pancreatitis.

Cholelithiasis

In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients-treated with semaglutide 0.5 mg and 1 mg respectively. Cholelithiasis was not reported in placebo-treated patients.

Fatigue, Dysgeusia and Dizziness

Other adverse reactions with a frequency of >0.4% associated with semaglutide include fatigue, dysgeusia and dizziness.

4.9 Overdose

Overdoses of up to 4 mg in a single dose, and up to 4 mg in a week have been reported in clinical trials. The most commonly reported adverse event was nausea. All patients recovered without complications.

There is no specific antidote for overdose with Ozempic. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of Ozempic of approximately 1 week (see section 5.2 Pharmacokinetic Properties).

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Drugs used in diabetes, Glucagon-like peptide-1 (GLP-1) analogues, ATC code: A10BJ06.

Mechanism of action

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system. The glucose and appetite effects are specifically mediated via GLP-1 receptors in the pancreas and the brain. GLP-1 receptors are also expressed in the heart, vasculature and immune system and kidney from where it may mediate cardiovascular and microvascular effects.

Compared to native GLP-1, semaglutide has a prolonged half-life of around 1 week making it suitable for once weekly s.c. administration. The principal mechanism of protraction is albumin binding, which results in decreased renal clearance and protection from metabolic degradation. Furthermore, semaglutide is stabilised against degradation by the DPP-4 enzyme.

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. During hypoglycaemia semaglutide diminishes insulin secretion and does not impair glucagon secretion.

Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite, which includes increased satiety and reduced hunger, as well as improved control of eating and decreased food cravings. Insulin resistance is also reduced, probably through reduction in body weight. In addition, semaglutide reduces the preference for high fat foods. Semaglutide had a beneficial effect on plasma lipids, lowered systolic blood pressure and reduced inflammation in clinical studies.

In animal studies, semaglutide attenuates the development of atherosclerosis by preventing aortic plaque progression and reducing inflammation in the plaque.

Pharmacodynamic Effects

All pharmacodynamic evaluations were performed after 12 weeks of treatment (including dose escalation) at steady state with semaglutide 1 mg once weekly.

Fasting and Postprandial Glucose

Semaglutide reduces fasting and postprandial glucose concentrations. In patients with type 2 diabetes, treatment with semaglutide 1 mg resulted in reductions in glucose in terms of absolute change from baseline (mmol/L/mg/dL) and relative reduction compared to placebo (%) for fasting glucose (1.6 mmol/L/29 mg/dL; 22%), 2 hour postprandial glucose (4.1 mmol/L/74 mg/dL; 37%), mean 24 hour glucose concentration (1.7 mmol/L/30 mg/dL; 22% reduction) and postprandial glucose excursions over 3 meals (0.6–1.1 mmol/L/11–20 mg/dL) compared to placebo (see Figure 2).

Semaglutide lowered fasting glucose after the first dose.

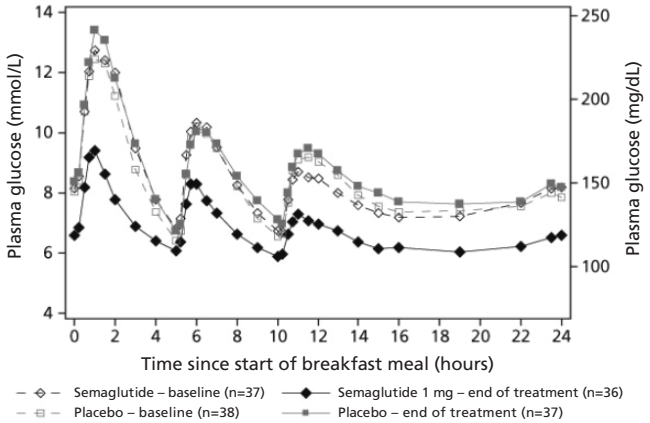


Figure 2: Mean 24 hour plasma glucose profiles (standardised meals) in patients with type 2 diabetes before (baseline) and after 12 weeks of treatment with semaglutide or placebo

Beta-cell function and insulin secretion

Semaglutide improves beta-cell function. Semaglutide, compared to placebo, improved first- and second-phase insulin response, with a 3- and 2-fold increase, respectively, following an intravenous bolus of glucose, and increased maximal beta-cell secretory capacity after an arginine stimulation test in patients with type 2 diabetes. In addition, semaglutide treatment increased fasting insulin concentrations compared to placebo.

Glucagon Secretion

Semaglutide lowers the fasting and postprandial glucagon concentrations. In patients with type 2 diabetes, semaglutide resulted in the following relative reductions in glucagon compared to placebo: fasting glucagon (8–21%), postprandial glucagon response (14–15%) and mean 24 hour glucagon concentration (12%).

Glucose Dependent Insulin and Glucagon Secretion

Semaglutide lowered high blood glucose concentrations by stimulating insulin secretion and lowering glucagon secretion in a glucose dependent manner. With semaglutide, the insulin secretion rate in patients with type 2 diabetes was comparable to that of healthy subjects (see Figure 3).

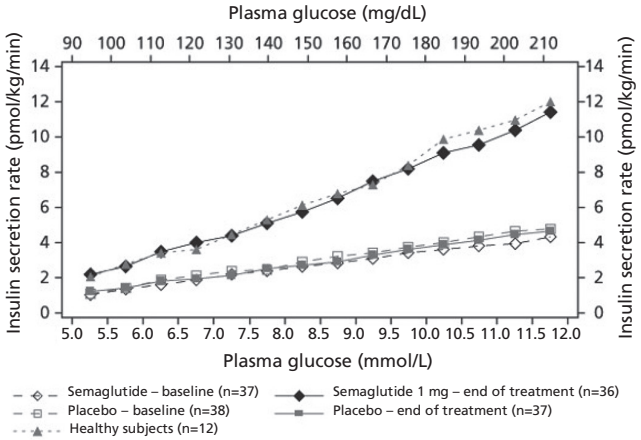


Figure 3: Mean insulin secretion rate versus glucose concentration in patients with type 2 diabetes during graded glucose infusion before (baseline) and after 12 weeks of treatment with semaglutide or placebo and in untreated healthy subjects

During induced hypoglycaemia, semaglutide compared to placebo did not alter the counter regulatory responses of increased glucagon, and did not impair the decrease of C-peptide in patients with type 2 diabetes.

Gastric Emptying

Semaglutide caused a minor delay of early postprandial gastric emptying, thereby reducing the rate at which glucose appears in the circulation postprandially.

Body Weight and Body Composition

A greater reduction in body weight was observed with semaglutide compared to studied comparators (placebo, sitagliptin, exenatide ER and insulin glargine) (section 5.1 Pharmacodynamic Properties). The body weight loss with semaglutide was predominantly from fat tissue with loss of fat mass being 3-fold larger than loss of lean mass.

Appetite, Energy Intake and Food Choice

Semaglutide compared to placebo lowered the energy intake of 3 consecutive *ad libitum* meals by 18–35%. This was supported by a semaglutide-induced suppression of appetite in the fasting state as well as postprandially, improved control of eating, less food cravings and a relative lower preference for high fat food.

Fasting and Postprandial Lipids

Semaglutide compared to placebo lowered fasting triglyceride and VLDL cholesterol concentrations by 12% and 21%, respectively. The postprandial triglyceride and VLDL cholesterol response to a high fat meal was reduced by >40%.

Cardiac Electrophysiology (QTc)

The effect of semaglutide on cardiac repolarization was tested in a thorough QTc trial. Semaglutide did not prolong QTc intervals at supra-therapeutic dose levels (up to 1.5 mg at steady state).

Clinical trials

Both improvement of glycaemic control and reduction of cardiovascular morbidity and mortality are an integral part of the treatment of type 2 diabetes.

The efficacy and safety of Ozempic 0.5 mg and 1 mg once weekly were evaluated in six randomised controlled phase 3a trials. Of these, five trials (SUSTAIN 1–5) had glycaemic efficacy assessment as the primary objective, while one trial (SUSTAIN 6) had cardiovascular outcome as the primary objective. Additionally, two phase 3 trials were conducted with Ozempic in Japanese patients with safety as the primary objective and efficacy the secondary objective.

The trials included in total 8,124 randomised patients with type 2 diabetes (4,792 treated with semaglutide).

An additional trial including 1,201 patients was conducted to compare the efficacy and safety of Ozempic 0.5 mg and 1 mg once weekly versus dulaglutide 0.75 mg and 1.5 mg once weekly, respectively.

Treatment with Ozempic demonstrated statistically significant and clinically meaningful reductions in HbA_{1c} (see Figure 4) and body weight maintained for up to 2 years compared to placebo and active control treatment (sitagliptin, insulin glargine, exenatide ER and dulaglutide).

The efficacy of Ozempic was not impacted by age, gender, race, ethnicity, BMI at baseline, body weight (kg) at baseline, diabetes duration and level of renal function impairment.

SUSTAIN 1 – Monotherapy

In a 30-week double-blind trial, 388 patients inadequately controlled with diet and exercise were randomised to Ozempic 0.5 mg or Ozempic 1 mg once weekly or placebo.

Patients had a mean age of 54 years and a mean duration of type 2 diabetes of 4.2 years. There were 64% White patients, 8% were Black or African Americans and 21% were Asian. For ethnicity, 30% of patients (n=115) were Hispanic or Latino. The mean BMI was 33 kg/m^2.

Table 3: Results at 30 weeks, monotherapy trial (SUSTAIN 1)

	Ozempic 0.5 mg	Ozempic 1 mg	Placebo
Intent-to-Treat (ITT) Population (N)	128	130	129
HbA_{1c} (%)			
Baseline (mean)	8.1	8.1	8.0
Change from baseline at week 30	-1.5	-1.6	0
Difference from placebo [95% CI]	-1.4 [-1.7; -1.1][a]	-1.5 [-1.8; -1.2][a]	–
Patients (%) achieving HbA_{1c} <7%	74[b]	72[b]	25
Patients (%) achieving HbA_{1c} ≤6.5%	59[b]	60[b]	13
FPG (mmol/L)			
Baseline (mean)	9.7	9.9	9.7
Change from baseline at week 30	-2.5	-2.3	-0.6
Difference from placebo [95% CI]	-2.0 [-2.5; -1.4][b]	-1.8 [-2.3; -1.3][b]	–
Body weight (kg)			
Baseline (mean)	89.8	96.9	89.1
Change from baseline at week 30	-3.7	-4.5	-1.0
Difference from placebo [95% CI]	-2.7 [-3.9; -1.6][a]	-3.6 [-4.7; -2.4][a]	–
Patients (%) achieving weight loss ≥5%	37[b]	45[b]	7
Patients (%) achieving weight loss ≥10%	8[c]	13[c]	2

[a] p <0.0001 (2-sided) for superiority, adjusted for multiplicity based on hierarchical testing of HbA_{1c} and body weight
[b] p <0.0001 for treatment difference, unadjusted for multiplicity
[c] p <0.05 for treatment difference, unadjusted for multiplicity

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Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.