

1. Name of the medicinal product**Ozempic®**

1.34 mg/ml

0.25 mg, 0.5 mg/dose

Solution for injection in pre-filled pen

2. Qualitative and quantitative composition

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

*Human glucagon-like peptide-1 (GLP-1) analogue produced in *Saccharomyces cerevisiae* cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection.

Clear and colourless or almost colourless, isotonic solution; pH=7.4.

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 in addition to metformin, metformin and sulphonylurea, metformin and basal insulin, or sodium-glucose cotransporter 2 (SGLT2) inhibitor.

For trial results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1.

4.2 Posology and method of administrationPosology

The starting dose is 0.25 mg semaglutide 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.

Semaglutide 0.25 mg is not a maintenance dose. Weekly doses higher than 1 mg are not recommended.

When Ozempic® is added to existing metformin therapy or to a SGLT2 inhibitor, the current dose of metformin or SGLT2 inhibitor can be continued unchanged.

When Ozempic® is added to existing therapy of sulphonylurea or insulin, a reduction in the dose of sulphonylurea or insulin should be considered to reduce the risk of hypoglycaemia (see sections 4.4 and 4.8).

Self-monitoring of blood glucose is not needed in order to adjust the dose of Ozempic®. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea and insulin, particularly when Ozempic® is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.

Missed dose

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.

Changing the dosing day

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.

Special populations

Elderly

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

Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease (see section 5.2).

Hepatic impairment

No dose adjustment is required for patients with 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 (see section 5.2).

Paediatric population

The safety and efficacy of semaglutide in children and adolescents below 18 years have not yet been established. No data are available.

Method of administration

Subcutaneous use.

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.

Ozempic® is to be administered once weekly at any time of the day, with or without meals.

For further information on administration, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

General

Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Semaglutide is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients whom had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started (see section 4.2).

There is no experience in patients with congestive heart failure NYHA class IV and semaglutide is therefore not recommended in these patients.

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 (see section 4.8).

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, semaglutide should be discontinued; if confirmed, semaglutide should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Hypoglycaemia

Patients treated with semaglutide 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 semaglutide (see section 4.8).

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). Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin. These patients should be monitored closely and treated according to clinical guidelines. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Semaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption.

Paracetamol

Semaglutide delays the rate of gastric emptying as assessed by paracetamol pharmacokinetics during a standardised meal test. Paracetamol $AUC_{0-60\text{min}}$ and C_{max} were decreased by 27% and 23%, respectively, following concomitant use of semaglutide 1 mg. The total paracetamol exposure (AUC_{0-5h}) was not affected. No dose adjustment of paracetamol is necessary when administered with semaglutide.

Oral contraceptives

Semaglutide is not anticipated to decrease the effect 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 the 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 (INR) were not affected in a clinically relevant manner. However, upon initiation of semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of INR is recommended.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential are recommended to use contraception when treated with semaglutide.

Pregnancy

Studies in animals have shown reproductive toxicity (see section 5.3). There are limited data from the use of semaglutide in pregnant women. Therefore, semaglutide should not be used during pregnancy. 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 5.2).

Breast-feeding

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

Fertility

The effect of semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats. 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 (see section 5.3).

4.7 Effects on ability to drive and use machines

Semaglutide 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 (see section 4.4).

4.8 Undesirable effects

Summary of safety profile

In 8 phase 3a trials 4,792 patients were exposed to semaglutide. The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea (very common), diarrhoea (very common) and vomiting (common). In general, these reactions were mild or moderate in severity and of short duration.

Tabulated list of adverse reactions

Table 1 lists adverse reactions identified in all phase 3 trials (including the long-term cardiovascular outcomes trial) and post-marketing reports in patients with type 2 diabetes mellitus (further described in section 5.1). The frequencies of the adverse reactions (except diabetic retinopathy complications, see footnote in Table 1) are based on a pool of the phase 3a trials excluding the cardiovascular outcomes trial (see text below the table for additional details).

The reactions are listed below by system organ class and absolute frequency. Frequencies are defined as: very common: ($\geq 1/10$); common: ($\geq 1/100$ to $< 1/10$); uncommon: ($\geq 1/1\ 000$ to $< 1/100$); rare: ($\geq 1/10\ 000$ to $< 1/1\ 000$); very rare: ($< 1/10\ 000$) and not known: cannot be estimated from available data. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 Frequency of adverse reactions of semaglutide

MedDRA system organ class	Very common	Common	Uncommon	Rare	Not known
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 oral antidiabetics (OAD) 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 Delayed gastric emptying		
Hepatobiliary disorders		Cholelithiasis			
Skin and subcutaneous tissue disorders					Angioedema ^d
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: retinal photocoagulation, treatment with intravitreal agents, vitreous haemorrhage, diabetes-related blindness (uncommon). Frequency based on cardiovascular outcomes trial.

^{c)} Grouped term covering also adverse events related to hypersensitivity such as rash and urticaria.

^{d)} From post-marketing reports.

2-year cardiovascular outcomes and safety trial

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

Description of selected adverse reactions

Hypoglycaemia

Severe hypoglycaemia was primarily observed when semaglutide 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 episodes (0.1% of subjects, 0.001 events/patient year) were observed with semaglutide in combination with oral antidiabetics other than sulfonylureas.

American Diabetes Association (ADA) classified hypoglycaemia occurred in 11.3% (0.3 events/patient year) of patients when semaglutide 1 mg was added to SGLT2 inhibitor in SUSTAIN 9 compared to 2.0% (0.04 events/patient year) of placebo-treated patients. Severe hypoglycaemia was reported in 0.7% (0.01 events/patient year) and 0% of patients, respectively.

Gastrointestinal adverse reactions

Nausea occurred in 17% and 19.9% of patients when treated with semaglutide 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% of patients. 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.

In concomitant use with an SGLT2 inhibitor in SUSTAIN 9, constipation and gastro-oesophageal reflux disease occurred in 6.7% and 4% respectively of patients treated with semaglutide 1 mg compared to no events for placebo-treated patients. The prevalence of these events did not decrease over time.

Acute pancreatitis

The frequency of adjudication-confirmed acute pancreatitis reported in phase 3a clinical trials was 0.3% for semaglutide and 0.2% for the comparator, respectively. In the 2-year cardiovascular outcomes trial the frequency of acute pancreatitis confirmed by adjudication was 0.5% for semaglutide and 0.6% for placebo (see section 4.4).

Diabetic retinopathy complications

A 2-year clinical trial investigated 3,297 patients with type 2 diabetes, with high cardiovascular risk, long duration of diabetes and poorly controlled blood glucose. In this trial, adjudicated events of diabetic retinopathy complications occurred in more patients treated with semaglutide (3%) compared to placebo (1.8%). This was observed in insulin-treated patients with known diabetic retinopathy. The treatment difference appeared early and persisted throughout the trial. Systematic evaluation of diabetic retinopathy complication was only performed in the cardiovascular outcomes trial. In clinical trials up to 1 year involving 4,807 patients with type 2 diabetes, adverse events related to diabetic retinopathy were reported in similar proportions of subjects treated with semaglutide (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, vs. 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. 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 (1-3%) 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 Ozempic®. In a long-term trial in subjects with cardiovascular risk factors, 16% of Ozempic®-treated subjects had an increase in heart rate of >10 bpm compared to 11% of subjects on placebo after 2 years of treatment.

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 reaction was nausea. All patients recovered without complications.

There is no specific antidote for overdose with semaglutide. 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 semaglutide of approximately 1 week (see section 5.2).

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 selectively 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.

Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. 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. In addition, semaglutide reduces the preference for high fat foods.

GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. 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) and relative reduction compared to placebo (%) for fasting glucose (1.6 mmol/L; 22% reduction), 2 hour postprandial glucose (4.1 mmol/L; 37% reduction), mean 24 hour glucose concentration (1.7 mmol/L; 22% reduction) and postprandial glucose excursions over 3 meals (0.6–1.1 mmol/L) compared with placebo. Semaglutide lowered fasting glucose after the first dose.

Beta-cell function and insulin secretion

Semaglutide improves beta-cell function. Compared to placebo, semaglutide improved first- and second-phase insulin response with a 3- and 2-fold increase, respectively, and increased maximal beta-cell secretory capacity 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.

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.

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 very low-density lipoproteins (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 dose levels up to 1.5 mg at steady state.

Clinical efficacy and safety

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 semaglutide 0.5 mg and 1 mg once weekly were evaluated in six randomised controlled phase 3a trials that included 7,215 patients with type 2 diabetes mellitus (4,107 treated with semaglutide). Five trials (SUSTAIN 1–5) had the glycaemic efficacy assessment as the primary objective, while one trial (SUSTAIN 6) had cardiovascular outcome as the primary objective.

In addition, a phase 3b trial (SUSTAIN 7) including 1,201 patients was conducted to compare the efficacy and safety of semaglutide 0.5 mg and 1 mg once weekly to dulaglutide 0.75 mg and 1.5 mg once weekly, respectively. A phase 3b trial (SUSTAIN 9), was conducted to investigate the efficacy and safety of semaglutide as add-on to SGLT2 inhibitor treatment.

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

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

In addition, a phase 3b trial (SUSTAIN 11), was conducted to investigate the effect of semaglutide vs. insulin aspart, both as add-on to metformin and optimised insulin glargine (U100).

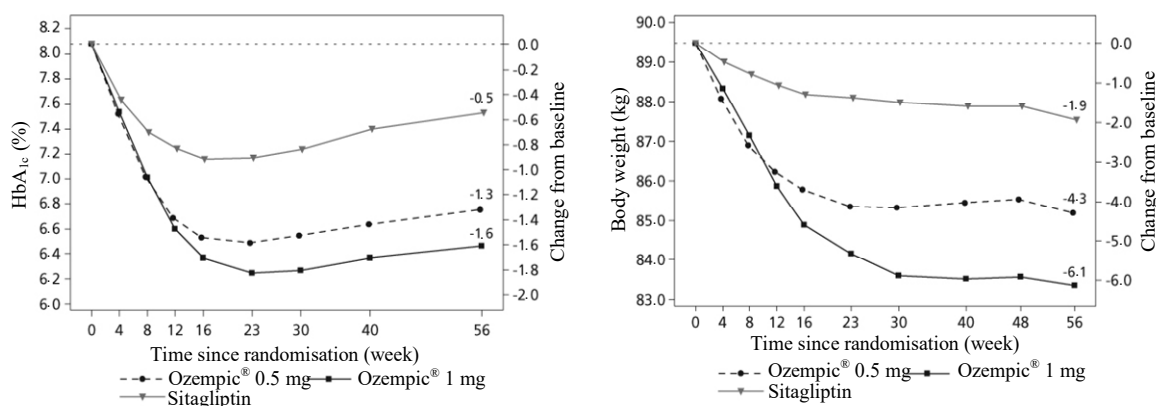
Detailed information is provided below.

SUSTAIN 2 – Semaglutide vs. sitagliptin both in combination with 1–2 oral antidiabetic medicinal products (metformin and/or thiazolidinediones)

In a 56-week active-controlled double-blind trial, 1,231 patients were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or sitagliptin 100 mg once daily, all in combination with metformin (94%) and/or thiazolidinediones (6%).

Table 2 SUSTAIN 2: Results at week 56

	Semaglutide 0.5 mg	Semaglutide 1 mg	Sitagliptin 100 mg
Intent-to-Treat (ITT) Population (N)	409	409	407
HbA_{1c} (%)			
Baseline (mean)	8.0	8.0	8.2
Change from baseline at week 56	-1.3	-1.6	-0.5
Difference from sitagliptin [95% CI]	-0.8 [-0.9, -0.6] ^a	-1.1 [-1.2, -0.9] ^a	-
Patients (%) achieving HbA_{1c} <7%	69	78	36
FPG (mmol/L)			
Baseline (mean)	9.3	9.3	9.6
Change from baseline at week 56	-2.1	-2.6	-1.1
Body weight (kg)			
Baseline (mean)	89.9	89.2	89.3
Change from baseline at week 56	-4.3	-6.1	-1.9
Difference from sitagliptin [95% CI]	-2.3 [-3.1, -1.6] ^a	-4.2 [-4.9, -3.5] ^a	-

^ap <0.0001 (2-sided) for superiority

Figure 1 Mean change in HbA_{1c} (%) and body weight (kg) from baseline to week 56

SUSTAIN 7 – Semaglutide vs. dulaglutide both in combination with metformin

In a 40-week, open-label trial, 1,201 patients on metformin were randomised 1:1:1:1 to once weekly semaglutide 0.5 mg, dulaglutide 0.75 mg, semaglutide 1 mg or dulaglutide 1.5 mg, respectively.

The trial compared 0.5 mg of semaglutide to 0.75 mg of dulaglutide and 1 mg of semaglutide to 1.5 mg of dulaglutide.

Gastrointestinal disorders were the most frequent adverse events, and occurred in similar proportion of patients receiving semaglutide 0.5 mg (129 patients [43%]), semaglutide 1 mg (133 [44%]), and dulaglutide 1.5 mg (143 [48%]); fewer patients had gastrointestinal disorders with dulaglutide 0.75 mg (100 [33%]).

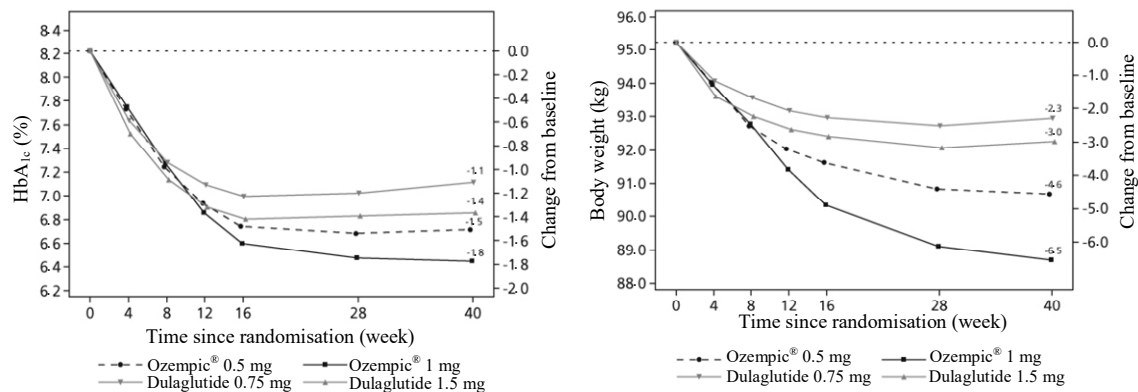
At week 40, the increase in pulse rate for semaglutide (0.5 mg and 1 mg) and dulaglutide (0.75 mg and 1.5 mg) was 2.4, 4.0, and 1.6, 2.1, beats/min, respectively.

Table 3 SUSTAIN 7: Results at week 40

	Semaglutide 0.5 mg	Semaglutide 1 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Intent-to-Treat (ITT) Population (N)	301	300	299	299
HbA_{1c} (%)				
Baseline (mean)	8.3	8.2	8.2	8.2
Change from baseline at week 40	-1.5	-1.8	-1.1	-1.4
Difference from dulaglutide [95% CI]	-0.4 ^b [-0.6, -0.2] ^a	-0.4 ^c [-0.6, -0.3] ^a	-	-
Patients (%) achieving HbA_{1c} <7%	68	79	52	67
FPG (mmol/L)				
Baseline (mean)	9.8	9.8	9.7	9.6
Change from baseline at week 40	-2.2	-2.8	-1.9	-2.2
Body weight (kg)				
Baseline (mean)	96.4	95.5	95.6	93.4
Change from baseline at week 40	-4.6	-6.5	-2.3	-3.0
Difference from dulaglutide [95% CI]	-2.3 ^b [-3.0, -1.5] ^a	-3.6 ^c [-4.3, -2.8] ^a	-	-

^ap <0.0001 (2-sided) for superiority

^bSemaglutide 0.5 mg vs. dulaglutide 0.75 mg

^cSemaglutide 1 mg vs. dulaglutide 1.5 mg

Figure 2 Mean change in HbA_{1c} (%) and body weight (kg) from baseline to week 40

SUSTAIN 3 – Semaglutide vs. exenatide ER both in combination with metformin or metformin with sulfonylurea

In a 56-week open-label trial, 813 patients on metformin alone (49%), metformin with sulfonylurea (45%) or other (6%) were randomised to semaglutide 1 mg or exenatide ER 2 mg once weekly.

Table 4 SUSTAIN 3: Results at week 56

	Semaglutide 1 mg	Exenatide ER 2 mg
Intent-to-Treat (ITT) Population (N)	404	405
HbA_{1c} (%)		
Baseline (mean)	8.4	8.3
Change from baseline at week 56	-1.5	-0.9
Difference from exenatide [95% CI]	-0.6 [-0.8, -0.4] ^a	-
Patients (%) achieving HbA_{1c} <7%	67	40
FPG (mmol/L)		
Baseline (mean)	10.6	10.4
Change from baseline at week 56	-2.8	-2.0
Body weight (kg)		
Baseline (mean)	96.2	95.4
Change from baseline at week 56	-5.6	-1.9
Difference from exenatide [95% CI]	-3.8 [-4.6, -3.0] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 4 – Semaglutide vs. insulin glargine both in combination with 1–2 oral antidiabetic medicinal products (metformin or metformin and sulfonylurea)

In a 30-week open-label comparator trial 1,089 patients were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly, or insulin glargine once-daily on a background of metformin (48%) or metformin and sulfonylurea (51%).

Table 5 SUSTAIN 4: Results at week 30

	Semaglutide 0.5 mg	Semaglutide 1 mg	Insulin Glargine
Intent-to-Treat (ITT) Population (N)	362	360	360
HbA_{1c} (%)			
Baseline (mean)	8.1	8.2	8.1
Change from baseline at week 30	-1.2	-1.6	-0.8
Difference from insulin glargine [95% CI]	-0.4 [-0.5, -0.2] ^a	-0.8 [-1.0, -0.7] ^a	-
Patients (%) achieving HbA_{1c} <7%	57	73	38
FPG (mmol/L)			
Baseline (mean)	9.6	9.9	9.7
Change from baseline at week 30	-2.0	-2.7	-2.1
Body weight (kg)			
Baseline (mean)	93.7	94.0	92.6
Change from baseline at week 30	-3.5	-5.2	+1.2
Difference from insulin glargine [95% CI]	-4.6 [-5.3, -4.0] ^a	-6.34 [-7.0, -5.7] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 5 – Semaglutide vs. placebo both in combination with basal insulin

In a 30-week double-blind placebo-controlled trial, 397 patients inadequately controlled with basal insulin with or without metformin were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or placebo.

Table 6 SUSTAIN 5: Results at week 30

	Semaglutide 0.5 mg	Semaglutide 1 mg	Placebo
Intent-to-Treat (ITT) Population (N)	132	131	133
HbA_{1c} (%)			
Baseline (mean)	8.4	8.3	8.4
Change from baseline at week 30	-1.4	-1.8	-0.1
Difference from placebo [95% CI]	-1.4 [-1.6, -1.1] ^a	-1.8 [-2.0, -1.5] ^a	-
Patients (%) achieving HbA_{1c} <7%	61	79	11
FPG (mmol/L)			
Baseline (mean)	8.9	8.5	8.6
Change from baseline at week 30	-1.6	-2.4	-0.5
Body weight (kg)			
Baseline (mean)	92.7	92.5	89.9
Change from baseline at week 30	-3.7	-6.4	-1.4
Difference from placebo [95% CI]	-2.3 [-3.3, -1.3] ^a	-5.1 [-6.1, -4.0] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 9 – Semaglutide vs. placebo as add-on to SGLT2 inhibitor ± metformin or sulfonylurea

In a 30-week double-blind placebo-controlled trial, 302 patients inadequately controlled with SGLT2 inhibitor with or without metformin or sulfonylurea were randomised to semaglutide 1 mg once weekly or placebo.

Table 7 SUSTAIN 9: Results at week 30

	Semaglutide 1 mg	Placebo
Intent-to-Treat (ITT) Population (N)	151	151
HbA_{1c} (%)		
Baseline (mean)	8.0	8.1
Change from baseline at week 30	-1.5	-0.1
Difference from placebo [95% CI]	-1.4 [-1.6, -1.2] ^a	-
Patients (%) achieving HbA_{1c} <7%	78.7	18.7
FPG (mmol/L)		
Baseline (mean)	9.1	8.9
Change from baseline at week 30	-2.2	0.0
Body weight (kg)		
Baseline (mean)	89.6	93.8
Change from baseline at week 30	-4.7	-0.9
Difference from placebo [95% CI]	-3.8 [-4.7, -2.9] ^a	-

^ap < 0.0001 (2-sided) for superiority, adjusted regarding multiplicity based on hierarchical testing of the HbA_{1c} value and body weight

SUSTAIN 11 - Semaglutide vs. insulin aspart as add-on to insulin glargine + metformin

In a 52-week open-label trial, 1,748 subjects with inadequately controlled T2D after a 12-week run-in period on insulin glargine and metformin were randomised to 1:1 to receive either semaglutide once-weekly (0.5 mg or 1.0 mg) or insulin aspart three times daily. The

included population had a mean diabetes duration of 13.4 years and a mean HbA_{1c} of 8.6%, with a target HbA_{1c} of 6.5-7.5%.

Treatment with semaglutide resulted in reduction in HbA_{1c} at week 52 (-1.5% for semaglutide vs. -1.2% for insulin aspart).

The number of severe hypoglycaemic episodes in both treatment arms was low (4 episodes with semaglutide vs. 7 episodes with insulin aspart).

Mean baseline body weight decreased with semaglutide (-4.1 kg) and increased with insulin aspart (+2.8 kg) and the estimated treatment difference was -6.99 kg (95%CI -7.41 to -6.57) at week 52.

Combination with sulfonylurea monotherapy

In SUSTAIN 6 (see subsection “Cardiovascular disease”) 123 patients were on sulfonylurea monotherapy at baseline. HbA_{1c} at baseline was 8.2%, 8.4% and 8.4% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively. At week 30, the change in HbA_{1c} was -1.6%, -1.5% and 0.1% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively.

Combination with premix insulin ± 1–2 OADs

In SUSTAIN 6 (see subsection “Cardiovascular disease”) 867 patients were on premix insulin (with or without OAD(s)) at baseline. HbA_{1c} at baseline was 8.8%, 8.9% and 8.9% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively. At week 30, the change in HbA_{1c} was -1.3%, -1.8% and -0.4% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively.

Cardiovascular disease

In a 104-week double-blind trial (SUSTAIN 6), 3,297 patients with type 2 diabetes mellitus at high cardiovascular risk were randomised to either semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or corresponding placebo in addition to standard-of-care hereafter followed for 2 years. In total 98% of the patients completed the trial and the vital status was known at the end of the trial for 99.6% of the patients.

The trial population was distributed by age as: 1,598 patients (48.5%) ≥65 years, 321 (9.7%) ≥75 years, and 20 (0.6%) ≥85 years. There were 2,358 patients with normal or mild renal impairment, 832 with moderate and 107 with severe or end stage renal impairment. There were 61% males, the mean age was 65 years and mean BMI was 33 kg/m². The mean duration of diabetes was 13.9 years.

The primary endpoint was time from randomisation to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke.

The total number of primary component MACE endpoints was 254, including 108 (6.6%) with semaglutide and 146 (8.9%) with placebo. See figure 4 for results on primary and secondary cardiovascular endpoints. Treatment with semaglutide resulted in a 26% risk reduction in the primary composite outcome of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke. The total numbers of cardiovascular deaths, non-fatal

myocardial infarctions and non-fatal strokes were 90, 111, and 71, respectively, including 44 (2.7%), 47 (2.9%), and 27 (1.6%), respectively, with semaglutide (figure 4). The risk reduction in the primary composite outcome was mainly driven by decreases in the rate of non-fatal stroke (39%) and non-fatal myocardial infarction (26%) (figure 3).

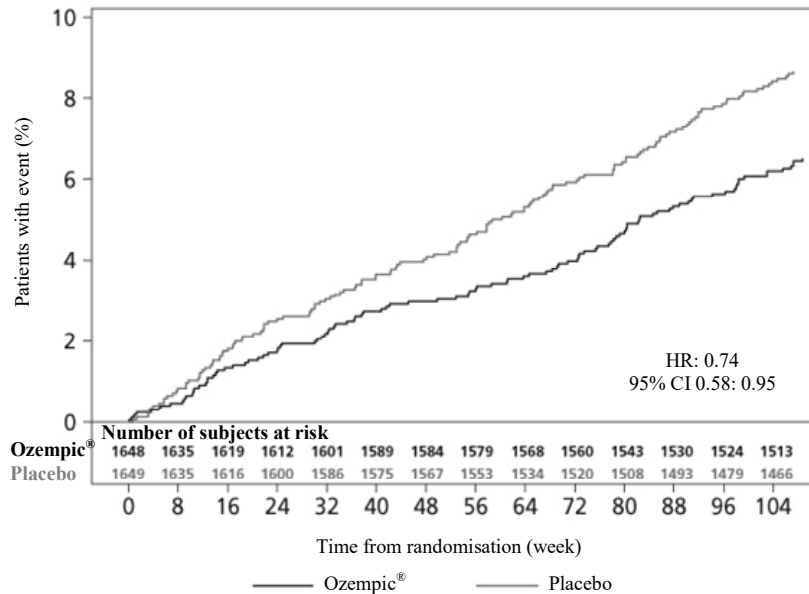


Figure 3 Kaplan-Meier plot of time to first occurrence of the composite outcome: cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (SUSTAIN 6)

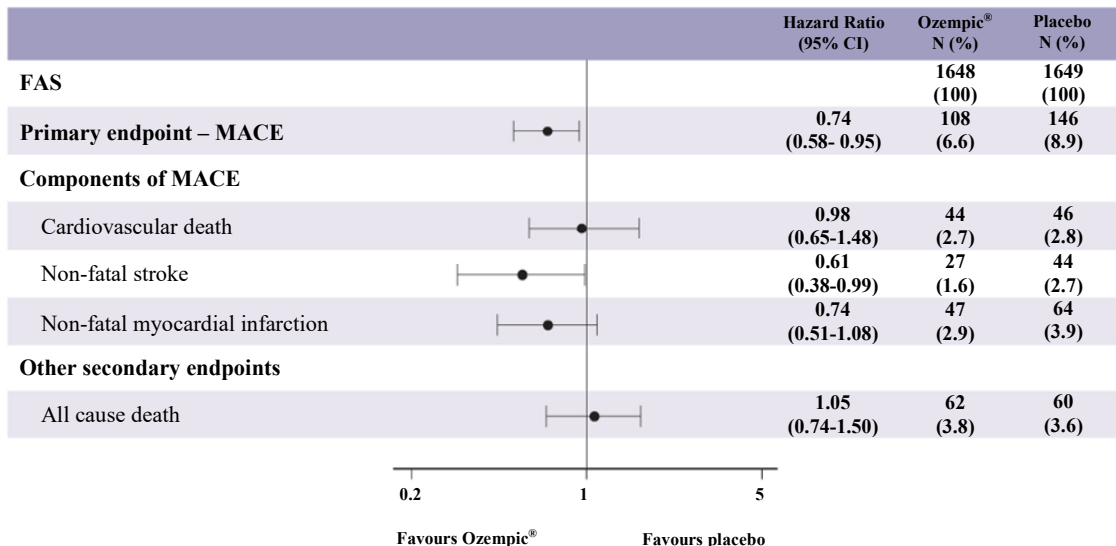


Figure 4 Forest plot: analyses of time to first occurrence of the composite outcome, its components and all cause death (SUSTAIN 6)

There were 158 events of new or worsening nephropathy. The hazard ratio [95% CI] for time to nephropathy (new onset of persistent macroalbuminuria, persistent doubling of serum

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creatinine, need for continuous renal replacement therapy and death due to renal disease) was 0.64 [0.46; 0.88] driven by new onset of persistent macroalbuminuria.

Body weight

After one year of treatment, a weight loss of $\geq 5\%$ and $\geq 10\%$ was achieved for more subjects with semaglutide 0.5 mg (46% and 13%) and 1 mg (52–62% and 21–24%) compared with the active comparators sitagliptin (18% and 3%) and exenatide ER (17% and 4%).

In the 40-week trial vs. dulaglutide a weight loss of $\geq 5\%$ and $\geq 10\%$ was achieved for more subjects with semaglutide 0.5 mg (44% and 14%) compared with dulaglutide 0.75 mg (23% and 3%) and semaglutide 1 mg (up to 63% and 27%) compared with dulaglutide 1.5 mg (30% and 8%).

A significant and sustained reduction in body weight from baseline to week 104 was observed with semaglutide 0.5 mg and 1 mg vs. placebo 0.5 mg and 1 mg, in addition to standard-of-care (-3.6 kg and -4.9 kg vs. -0.7 kg and -0.5 kg, respectively) in SUSTAIN 6.

Blood pressure

Significant reductions in mean systolic blood pressure were observed when semaglutide 0.5 mg (3.5–5.1 mmHg) and 1 mg (5.4–7.3 mmHg) were used in combination with oral antidiabetic medicinal products or basal insulin. For diastolic blood pressure, there were no significant differences between semaglutide and comparators.

5.2 Pharmacokinetic properties

Compared to native GLP-1, semaglutide has a prolonged half-life of around 1 week making it suitable for once weekly subcutaneous 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.

Absorption

Maximum concentration was reached 1 to 3 days post dose. Steady state exposure was achieved following 4–5 weeks of once weekly administration. In patients with type 2 diabetes, the mean steady state concentrations following subcutaneous administration of 0.5 mg and 1 mg semaglutide were approximately 16 nmol/L and 30 nmol/L, respectively. Semaglutide exposure increased in a dose proportional manner for doses of 0.5 mg and 1 mg. Similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm. Absolute bioavailability of subcutaneous semaglutide was 89%.

Distribution

The mean volume of distribution of semaglutide following subcutaneous administration in patients with type 2 diabetes was approximately 12.5 L. Semaglutide was extensively bound to plasma albumin (>99%).

Biotransformation

Prior to excretion, semaglutide is extensively metabolised through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain. The enzyme neutral endopeptidase (NEP) is expected to be involved in the metabolism of semaglutide.

Elimination

In a trial with a single subcutaneous dose of radiolabelled semaglutide, it was found that the primary excretion routes of semaglutide-related material were via urine and faeces; approximately 2/3 of semaglutide-related material were excreted in urine and approximately 1/3 in faeces. Approximately 3% of the dose was excreted as intact semaglutide via urine. In patients with type 2 diabetes clearance of semaglutide was approximately 0.05 L/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 weeks after the last dose.

Special population

Elderly

Age had no effect on the pharmacokinetics of semaglutide based on data from phase 3a studies including patients of 20–86 years of age.

Gender, race and ethnicity

Gender, race (White, Black or African-American, Asian) and ethnicity (Hispanic or Latino, non-Hispanic or -Latino) had no effect on the pharmacokinetics of semaglutide.

Body weight

Body weight has an effect on the exposure of semaglutide. Higher body weight results in lower exposure; a 20% difference in body weight between individuals will result in an approximate 16% difference in exposure. Semaglutide doses of 0.5 mg and 1 mg provide adequate systemic exposure over a body weight range of 40–198 kg.

Renal impairment

Renal impairment did not impact the pharmacokinetics of semaglutide in a clinically relevant manner. This was shown with a single dose of 0.5 mg semaglutide for patients with different degrees of renal impairment (mild, moderate, severe or patients in dialysis) compared with subjects with normal renal function. This was also shown for subjects with type 2 diabetes and with renal impairment based on data from phase 3a studies, although the experience in patients with end-stage renal disease was limited.

Hepatic impairment

Hepatic impairment did not have any impact on the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated in patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function in a trial with a single-dose of 0.5 mg semaglutide.

Paediatric population

Semaglutide has not been studied in paediatric patients.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeat-dose toxicity or genotoxicity.

Non-lethal thyroid C-cell tumours observed in rodents are a class effect for GLP-1 receptor agonists. In 2-year carcinogenicity studies in rats and mice, semaglutide caused thyroid C-cell tumours at clinically relevant exposures. No other treatment-related tumours were observed. The rodent C-cell tumours are caused by a non-genotoxic, specific GLP-1 receptor mediated mechanism to which rodents are particularly sensitive. The relevance for humans is considered to be low, but cannot be completely excluded.

In fertility studies in rats, semaglutide did not affect mating performance or male fertility. In female rats, an increase in oestrous cycle length and a small reduction in *corpora lutea* (ovulations) were observed at doses associated with maternal body weight loss.

In embryo-foetal development studies in rats, semaglutide caused embryotoxicity below clinically relevant exposures. Semaglutide caused marked reductions in maternal body weight and reductions in embryonic survival and growth. In foetuses, major skeletal and visceral malformations were observed, including effects on long bones, ribs, vertebrae, tail, blood vessels and brain ventricles. Mechanistic evaluations indicated that the embryotoxicity involved a GLP-1 receptor mediated impairment of the nutrient supply to the embryo across the rat yolk sac. Due to species differences in yolk sac anatomy and function, and due to lack of GLP-1 receptor expression in the yolk sac of non-human primates, this mechanism is considered unlikely to be of relevance to humans. However, a direct effect of semaglutide on the foetus cannot be excluded.

In developmental toxicity studies in rabbits and *cynomolgus* monkeys, increased pregnancy loss and slightly increased incidence of foetal abnormalities were observed at clinically relevant exposures. The findings coincided with marked maternal body weight loss of up to 16%. Whether these effects are related to the decreased maternal food consumption as a direct GLP-1 effect is unknown.

Postnatal growth and development were evaluated in *cynomolgus* monkeys. Infants were slightly smaller at delivery, but recovered during the lactation period.

In juvenile rats, semaglutide caused delayed sexual maturation in both males and females. These delays had no impact upon fertility and reproductive capacity of either sex, or on the ability of the females to maintain pregnancy.

6.1 List of excipients

Disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and water for injections.

6.2 Incompatibilities

In the absence of compatibility studies this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

36 months

Before first use

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Expiry date is stated on the pen label and carton after 'Expiry'.

After first opening

In-use shelf life: 6 weeks

Store below 30 °C or in a refrigerator (2 °C – 8 °C). Do not freeze Ozempic®. Keep the pen cap on when the pen is not in use in order to protect it from light.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Keep away from the cooling element.
Do not freeze Ozempic®.

Keep the pen cap on in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

1.5 ml glass cartridge (type I glass) closed at the one end with a rubber plunger (chlorobutyl) and at the other end with an aluminium cap with a laminated rubber sheet (bromobutyl/polyisoprene) inserted. The cartridge is assembled into a disposable pre-filled pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

Pack size

1 pre-filled pen and 6 disposable NovoFine® Plus needles.

Each pre-filled pen contains 1.5 ml of solution, delivering doses of 0.25 mg or 0.5 mg.

HARUS DENGAN RESEP DOKTER

Reg. No.: DKIXXXXXXXXXXXXX

6.6 Special precautions for disposal and other handling

The patient should be advised to discard the injection needle after each injection and store the pen without an injection needle attached. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.

The pen is for use by one person only.

Ozempic® should not be used if it does not appear clear and colourless or almost colourless.

Ozempic® should not be used if it has been frozen.

Ozempic® can be administered with needles up to a length of 8 mm. The pen is designed to be used with NovoFine® or NovoTwist® disposable needles. NovoFine® Plus needles are included in the package.

Any unused medicinal product and other waste material should be disposed of in accordance with local requirements.

7. Manufactured by:

Novo Nordisk A/S

Brennum Park

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DK-3400 Hillerød
Denmark

Released by:
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

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PT Beta Pharmacon
Indonesia

Distributed by:
PT Anugrah Argon Medica
Indonesia

Based on approval date: 22nd December 2023

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Novo Nordisk A/S

Ozempic®
1.34 mg/ml
0.25 mg, 0.5 mg/dose
solution for injection in pre-filled pen
semaglutide

Instructions on how to use Ozempic® 0.25 mg, 0.5 mg/dose solution for injection in pre-filled pen

Please read these instructions carefully before using your Ozempic® pre-filled pen.

Talk to your doctor, nurse or pharmacist about how to inject Ozempic® correctly.

Start by checking your pen to **make sure that it contains Ozempic® 0.25 mg, 0.5 mg/dose** then look at the illustrations below to get to know the different parts of your pen and needle.

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who knows how to use the Ozempic® pre-filled pen.

Your pen is a pre-filled dial-a-dose pen. It contains 2 mg of semaglutide, and you can select doses of 0.25 mg or 0.5 mg.

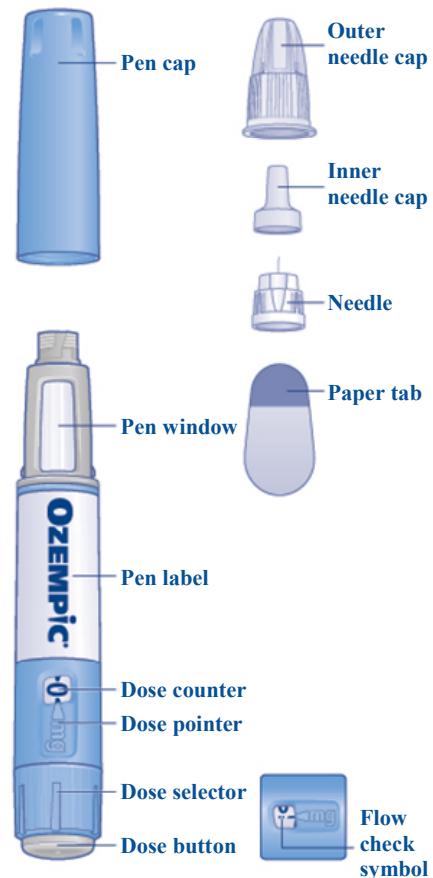
One unused pen contains:

- 4 doses of 0.25 mg (starting dose) *and* 2 doses of 0.5 mg
- **or** 4 doses of 0.5 mg

Use the table inside the lid of the carton to keep track of how many injections you have taken and when you took the injections.

Your pen is designed to be used with NovoFine® and NovoTwist® disposable needles up to a length of 8 mm. NovoFine® Plus needles are included in the pack.

Ozempic® pre-filled pen and needle (example)

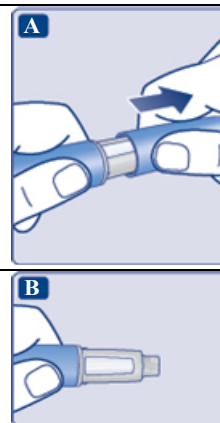


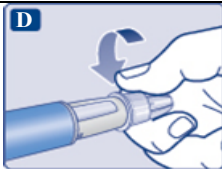
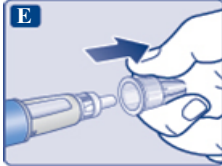
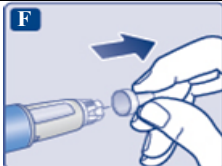
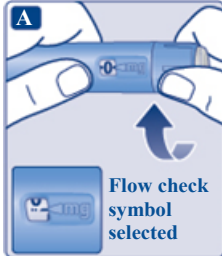
Important information

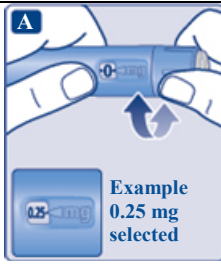
Pay special attention to these notes, as they are important for safe use of the pen.

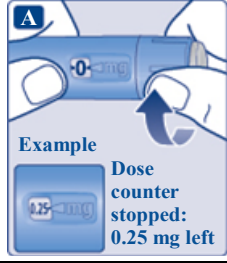
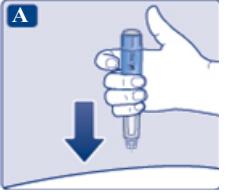
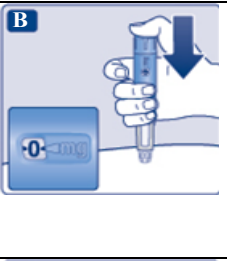
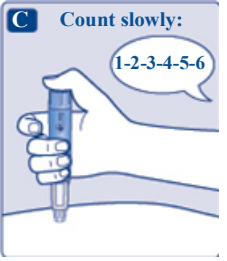
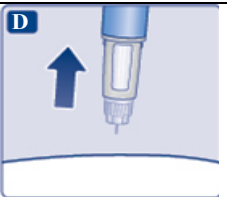
1. Prepare your pen with a new needle

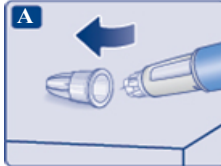
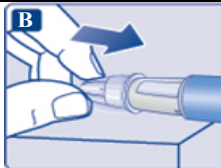
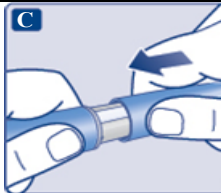
- **Check the name and coloured label** of your pen, to make sure that it contains Ozempic® 0.25 mg, 0.5 mg/dose. This is especially important if you take more than one type of injectable medicine. Using the wrong medicine could be harmful to your health.
- **Pull off the pen cap.**
- **Check that the solution in your pen is clear** and colourless. Look through the pen window. If the solution looks cloudy or coloured, do not use the pen.



• Take a new needle Check the paper tab and the outer needle cap for damages that could affect sterility. If any damage is seen use a new needle. • Tear off the paper tab.		
Make sure to attach the needle correctly. • Push the needle straight onto the pen. • Turn until it is on tight.		
The needle is covered by two caps. You must remove both caps. If you forget to remove both caps, you will not inject any solution. • Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen.		
• Pull off the inner needle cap and throw it away. If you try to put it back on, you may accidentally stick yourself with the needle. A drop of solution may appear at the needle tip. This is normal, but you must still check the flow, if you use a new pen for the first time. See step 2 'Check the flow with each new pen'. Do not attach a new needle to your pen until you are ready to take your injection.		
 Always use a new needle for each injection. This may prevent blocked needles, contamination, infection and inaccurate dosing.		
 Never use a bent or damaged needle.		
2. Check the flow with each new pen		
• If your pen is already in use, go to step 3 'Select your dose'. Only check the flow before your first injection with each new pen. • Turn the dose selector to the flow check symbol () right past '0'. Make sure the flow check symbol lines up with the pointer.		

Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter returns to '0'. The '0' must line up with the dose pointer. A drop of solution should appear at the needle tip.	
A small drop may remain at the needle tip, but it will not be injected. If no drop appears, repeat step 2 'Check the flow with each new pen' up to 6 times. If there is still no drop, change the needle and repeat step 2 'Check the flow with each new pen' once more. Dispose of the pen and use a new one if a drop of solution still does not appear.	
⚠ Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that the solution flows. If no drop appears, you will not inject any medicine even though the dose counter may move. This may indicate a blocked or damaged needle. If you do not check the flow before your first injection with each new pen, you may not get the prescribed dose and the intended effect of Ozempic®.	
3. Select your dose	
Turn the dose selector until the dose counter shows your prescribed dose (0.25 mg or 0.5 mg). If you select the wrong dose, you can turn the dose selector forwards or backwards to the correct dose. The pen can dial up to a maximum of 0.5 mg.	
The dose selector changes the dose. Only the dose counter and dose pointer will show how many mg you select per dose. You can select up to 0.5 mg per dose. When your pen contains less than 0.5 mg, the dose counter stops before 0.5 is shown. The dose selector clicks differently when turned forwards, backwards or past the number of mg left. Do not count the pen clicks.	
⚠ Always use the dose counter and the dose pointer to see how many mg you have selected before injecting this medicine. Do not count the pen clicks. Only doses of 0.25 mg or 0.5 mg must be selected with the dose selector. The selected dose must line up precisely with the dose pointer to ensure that you get a correct dose.	
How much solution is left	

• To see how much solution is left, use the dose counter: Turn the dose selector until the dose counter stops. If it shows 0.5, at least 0.5 mg is left in your pen. If the dose counter stops before 0.5 mg, there is not enough solution left for a full dose of 0.5 mg.	
⚠ If there is not enough solution left in your pen for a full dose, do not use it. Use a new Ozempic® pen.	
4. Inject your dose	
• Insert the needle into your skin as your doctor or nurse has shown you. • Make sure you can see the dose counter. Do not cover it with your fingers. This could interrupt the injection.	
• Press and hold down the dose button. Watch as the dose counter returns to '0'. The '0' must line up with the dose pointer. You may then hear or feel a click. • Continue pressing the dose button while keeping the needle in your skin.	
• Count slowly to 6, while keeping the dose button pressed. • If the needle is removed earlier, you may see a stream of solution coming from the needle tip. If so, the full dose will not be delivered.	
• Remove the needle from your skin. You can then release the dose button. If blood appears at the injection site, press lightly.	
You may see a drop of solution at the needle tip after injecting. This is normal and does not affect your dose.	
⚠ Always watch the dose counter to know how many mg you inject. Hold the dose button down until the dose counter returns to '0'. How to identify a blocked or damaged needle – If '0' does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle. – In this case, you have not received any medicine – even though the dose counter has moved from the original dose that you have set. How to handle a blocked needle	

Change the needle as described in step 5 'After your injection' and repeat all steps starting with step 1 'Prepare your pen with a new needle'. Make sure you select the full dose you need. Never touch the dose counter when you inject. This can interrupt the injection.	
5. After your injection	
Always dispose of the needle after each injection to ensure convenient injections and prevent blocked needles. If the needle is blocked, you will not inject any medicine. • Lead the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap.	
• Once the needle is covered, carefully push the outer needle cap completely on. • Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities.	
• Put the pen cap on your pen after each use to protect the solution from light.	
When the pen is empty, throw it away without a needle on as instructed by your doctor, nurse, pharmacist or local authorities.	
⚠ Never try to put the inner needle cap back on the needle. You may stick yourself with the needle. ⚠ Always remove the needle from your pen immediately after each injection. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.	
⚠ Further important information • Always keep your pen and needles out of the sight and reach of others, especially children. • Never share your pen or your needles with other people. • Caregivers must be very careful when handling used needles to prevent needle injury and cross-infection.	
Caring for your pen	
Treat your pen with care. Rough handling or misuse may cause inaccurate dosing. If this happens you might not get the intended effect of this medicine.	
• Do not leave the pen in a car or another place where it can get too hot or too cold. • Do not inject Ozempic® which has been frozen. If you do that, you might not get the intended effect of this medicine. • Do not inject Ozempic® which has been exposed to direct sunlight. If you do that, you might not get the intended effect of this medicine. • Do not expose your pen to dust, dirt or liquid. • Do not wash, soak or lubricate your pen. It may be cleaned with a mild detergent on a moistened cloth.	

- **Do not drop your pen** or knock it against hard surfaces. If you drop it or suspect a problem, attach a new needle and check the flow before you inject.
- **Do not try to refill your pen.** Once empty, it must be disposed of.
- **Do not try to repair your pen** or pull it apart.

Brosur kemasan: Informasi untuk pasien

Ozempic®

1,34 mg/ml

0,25 mg; 0,5 mg/dosis

**Larutan injeksi dalam pena yang sudah terisi
semaglutide**

Bacalah seluruh brosur ini dengan teliti sebelum Anda mulai menggunakan obat ini karena brosur ini berisi informasi yang penting untuk Anda.

- Simpan brosur ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini mungkin membahayakan mereka, meskipun jika mereka memiliki tanda – tanda sakit yang sama dengan Anda.
- Jika Anda mengalami efek samping apapun, bicarakan dengan dokter, apoteker atau perawat Anda. Termasuk kemungkinan efek samping apapun yang tidak tercantum dalam brosur ini. Lihat bagian 4.

Apa yang terdapat dalam brosur ini

1. Apa itu Ozempic® dan untuk apa kegunaannya
2. Apa yang Anda perlu ketahui sebelum menggunakan Ozempic®
3. Bagaimana cara menggunakan Ozempic®
4. Efek samping yang mungkin dirasakan
5. Bagaimana cara menyimpan Ozempic®
6. Isi kemasan dan informasi lain

1. Apa itu Ozempic® dan untuk apa kegunaannya

Ozempic® berisi zat aktif semaglutide. Zat aktif tersebut membantu tubuh Anda mengurangi kadar gula darah Anda hanya ketika kadar gula darah terlalu tinggi dan dapat membantu mencegah penyakit jantung.

Ozempic® digunakan untuk pengobatan orang dewasa (usia 18 tahun dan ke atas) dengan diabetes mellitus tipe 2 ketika diet dan olahraga bersama dengan obat – obat diabetes lain tidak cukup untuk mengontrol kadar gula darah Anda. Obat – obatan lain ini mungkin digunakan secara oral atau suntikan meliputi metformin, metformin dan sulfonilurea, metformin dan insulin basal, atau *sodium-glucose cotransporter 2 (SGLT2) inhibitor*.

Penting bahwa Anda terus melanjutkan rencana diet dan olahraga Anda sebagaimana yang diberitahu oleh dokter, apoteker atau perawat Anda.

2. Apa yang Anda perlu ketahui sebelum menggunakan Ozempic®

Jangan menggunakan Ozempic®

- jika Anda alergi terhadap semaglutide atau salah satu zat lain dari obat ini (yang tercantum dalam bagian 6).

Peringatan dan pencegahan

Bicarakan dengan dokter, apoteker atau perawat Anda sebelum menggunakan obat ini.

Obat ini tidak sama dengan insulin dan Anda seharusnya tidak menggunakannya jika:

- Anda memiliki diabetes tipe 1 – suatu kondisi dimana tubuh Anda tidak memproduksi insulin apapun
- Anda memiliki penyakit yang mengarah ke diabetes ketoasidosis – komplikasi diabetes dengan kadar gula darah yang tinggi, kesulitan bernapas, kebingungan, rasa haus yang berlebihan, bau manis di nafas atau rasa manis atau logam di mulut.

Ozempic® bukan insulin dan seharusnya tidak digunakan sebagai pengganti insulin.

Efek terhadap sistem pencernaan

Selama pengobatan dengan obat ini, Anda mungkin merasa mual atau muntah, atau diare. Efek samping tersebut dapat menyebabkan dehidrasi (kehilangan cairan). Penting untuk Anda minum cairan yang banyak untuk mencegah dehidrasi. Hal tersebut penting terutama jika Anda memiliki gangguan ginjal. Bicarakan dengan dokter Anda jika Anda memiliki pertanyaan atau pertimbangan.

Nyeri perut yang parah dan berkelanjutan yang dapat disebabkan oleh pankreatitis akut

Jika Anda mengalami nyeri yang parah dan berkelanjutan di daerah perut - langsung temui dokter karena hal tersebut dapat menjadi tanda pankreatitis akut (radang pankreas). Lihat bagian 4 untuk tanda – tanda peringatan radang pankreas.

Kadar gula darah yang rendah (hipoglikemia)

Mengkombinasikan sulfonilurea atau insulin dengan obat ini mungkin meningkatkan risiko terkena kadar gula darah yang rendah (hipoglikemia). Lihat bagian 4 untuk tanda – tanda peringatan dari kadar gula darah yang rendah. Dokter Anda mungkin meminta Anda untuk memeriksa kadar gula darah Anda. Hal tersebut akan membantu dokter memutuskan apakah dosis sulfonilurea atau insulin perlu diubah untuk mengurangi risiko kadar gula darah yang rendah.

Penyakit mata diabetes (retinopati)

Jika Anda memiliki penyakit mata diabetes dan sedang menggunakan insulin, obat ini mungkin menyebabkan memburuknya penglihatan Anda, dan mungkin memerlukan pengobatan. Beritahu dokter Anda jika Anda memiliki penyakit mata diabetes atau jika Anda mengalami gangguan mata selama pengobatan dengan obat ini.

Anak-anak dan remaja

Obat ini tidak direkomendasikan untuk anak-anak dan remaja usia di bawah 18 tahun karena keamanan dan khasiat dalam kelompok usia tersebut belum dikembangkan.

Obat – obatan lain dan Ozempic®

Beritahu dokter, apoteker atau perawat Anda jika Anda sedang mengonsumsi, baru-baru ini sudah mengonsumsi, atau mungkin mengonsumsi obat lain, termasuk obat – obatan herbal atau obat lain yang Anda beli tanpa resep.

Tidak ada penyesuaian dosis parasetamol, kontrasepsi oral, atorvastatin, digoksin dan metformin ketika digunakan bersama dengan semaglutide.

Secara khusus, beritahu dokter, apoteker atau perawat Anda jika Anda menggunakan obat – obatan yang mengandung salah satu zat berikut:

- Warfarin atau obat serupa lainnya yang dikonsumsi secara oral untuk mengurangi pembekuan darah (anti koagulan oral). Anda mungkin memerlukan pemeriksaan darah yang sering untuk memeriksa seberapa cepat darah Anda membeku.
- Jika Anda sedang menggunakan insulin, dokter Anda akan memberitahu Anda bagaimana cara mengurangi dosis insulin dan akan merekomendasikan Anda untuk lebih sering memantau kadar gula darah Anda untuk menghindari hiperglikemia (kadar gula darah yang tinggi) dan diabetes ketoasidosis (komplikasi diabetes yang terjadi ketika tubuh tidak dapat memecah glukosa karena tidak terdapat cukup insulin).

Kehamilan dan menyusui

Jika Anda sedang hamil atau menyusui, merasa Anda mungkin hamil, atau berencana untuk punya anak, mintalah saran kepada dokter Anda sebelum menggunakan obat ini.

Obat ini seharusnya tidak digunakan selama kehamilan, karena belum diketahui apakah obat ini memengaruhi janin. Oleh karena itu, penggunaan kontrasepsi direkomendasikan ketika menggunakan obat ini. Jika Anda ingin hamil, diskusikan bagaimana mengubah pengobatan Anda dengan dokter Anda karena Anda seharusnya berhenti menggunakan obat ini setidaknya 2 bulan sebelumnya. Jika Anda hamil ketika menggunakan obat ini, bicarakan dengan dokter Anda segera, karena pengobatan Anda akan perlu diubah.

Jangan menggunakan obat ini jika Anda sedang menyusui, karena belum diketahui apakah obat ini masuk ke dalam ASI.

Mengemudi dan menjalankan mesin

Ozempic® hampir tidak memengaruhi kemampuan Anda mengemudi atau menggunakan mesin. Jika Anda menggunakan obat ini dikombinasikan dengan sulfonilurea atau insulin, kadar gula darah yang rendah (hipoglikemia) dapat terjadi yang mungkin mengurangi kemampuan Anda untuk berkonsentrasi. Jangan mengemudi atau menjalankan mesin jika Anda mengalami tanda – tanda kadar gula darah yang rendah. Lihat bagian 2 '*Peringatan dan pencegahan*' untuk informasi tentang peningkatan risiko kadar gula darah yang rendah dan bagian 4 untuk tanda – tanda peringatan kadar gula darah yang rendah. Bicarakan dengan dokter Anda untuk informasi lebih lanjut.

Kandungan natrium

Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per dosis, pada dasarnya 'bebas natrium'.

3. Bagaimana cara menggunakan Ozempic®

Selalu gunakan obat ini sama seperti yang diberitahu oleh dokter Anda. Periksa dengan dokter, apoteker atau perawat Anda jika Anda tidak yakin.

Berapa banyak yang digunakan

- Dosis awal adalah 0,25 mg seminggu sekali selama empat minggu.
- Setelah empat minggu dokter Anda akan meningkatkan dosis menjadi 0,5 mg seminggu sekali.
- Dokter mungkin meningkatkan dosis Anda ke 1 mg seminggu sekali jika kadar gula darah Anda tidak terkontrol dengan cukup baik dengan dosis 0,5 mg seminggu sekali.

Jangan mengubah dosis Anda kecuali diberitahu oleh dokter Anda.

Bagaimana Ozempic® diberikan

Ozempic® diberikan sebagai suntikan di bawah kulit (injeksi subkutan). Jangan menyuntikkan ke dalam pembuluh darah atau otot.

- Tempat terbaik untuk penyuntikan adalah paha depan, bagian depan pinggang (perut), atau lengan atas Anda.
- Sebelum menggunakan pena untuk pertama kalinya, dokter atau perawat Anda akan menunjukkan kepada Anda bagaimana cara menggunakannya.

Instruksi penggunaan yang detail ada di sisi lain dari brosur kemasan ini.

Kapan menggunakan Ozempic®

- Anda seharusnya menggunakan obat ini seminggu sekali di hari yang sama setiap minggu jika memungkinkan.
- Anda dapat melakukan penyuntikan kapanpun sepanjang hari – tidak tergantung makanan.

Untuk membantu mengingatkan Anda melakukan penyuntikan obat ini seminggu sekali saja, direkomendasikan untuk mencatat hari kerja sebagai pilihan (misalnya Rabu) di karton dan menulis tanggal di karton setiap kali Anda sudah menyuntikkannya.

Jika perlu Anda dapat mengubah hari penyuntikan mingguan Anda dari obat ini selama sudah berjalan setidaknya 3 hari sejak penyuntikan terakhir Anda. Setelah memilih hari yang baru, lanjutkan dengan dosis seminggu sekali.

Jika Anda menggunakan Ozempic® lebih banyak dari yang seharusnya

Jika Anda menggunakan Ozempic® lebih banyak dari yang seharusnya, langsung bicarakan dengan dokter Anda. Anda mungkin mengalami efek samping seperti perasaan mual.

Jika Anda lupa untuk menggunakan Ozempic®

Jika Anda lupa menyuntikkan satu dosis dan:

- sudah 5 hari atau kurang dari yang Anda seharusnya menggunakan Ozempic®, gunakan sesegera mungkin setelah Anda ingat. Kemudian suntikkan dosis berikutnya seperti biasa di hari yang sudah Anda jadwalkan.

- sudah lebih dari 5 hari sejak Anda seharusnya menggunakan Ozempic®, lewati dosis yang terlupa. Kemudian suntikkan dosis berikutnya seperti biasa di hari yang sudah Anda jadwalkan.

Jangan menggunakan dosis ganda untuk mengganti dosis yang terlupa.

Jika Anda berhenti menggunakan Ozempic®

Jangan berhenti menggunakan obat ini tanpa berbicara dengan dokter Anda. Jika Anda berhenti menggunakannya, kadar gula darah Anda mungkin naik.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter, apoteker atau perawat Anda.

4. Efek samping yang mungkin dirasakan

Seperti semua obat – obatan, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping yang serius

Umum (mungkin memengaruhi hingga 1 dari 10 orang)

- komplikasi dari penyakit mata diabetes (retinopati) - Anda seharusnya memberitahu dokter Anda jika Anda mengalami gangguan mata, seperti perubahan di pandangan, selama pengobatan dengan obat ini.

Tidak umum (mungkin memengaruhi hingga 1 dari 100 orang)

- inflamasi pankreas (pankreatitis akut) yang dapat menyebabkan nyeri parah di lambung dan punggung yang tidak hilang. Anda seharusnya segera ke dokter jika Anda mengalami gejala tersebut.

Jarang (mungkin memengaruhi hingga 1 dari 1.000 orang)

- reaksi alergi yang parah (reaksi anafilaksis, angioedema). Anda harus segera mendapatkan bantuan medis dan langsung menginformasikan dokter Anda jika Anda mendapatkan gejala seperti gangguan pernapasan, pembengkakan di wajah, bibir, lidah dan/atau tenggorokan dengan kesulitan menelan dan detak jantung yang cepat.

Efek samping lain

Sangat umum (mungkin memengaruhi lebih dari 1 dari 10 orang)

- mual – biasanya hilang seiring waktu
- diare – biasanya hilang seiring waktu.
- kadar gula yang rendah (hipoglikemia) ketika obat ini digunakan dengan obat yang mengandung sulfonilurea atau insulin

Umum (mungkin memengaruhi hingga 1 dari 10 orang)

- muntah
- kadar gula darah yang rendah (hipoglikemia) ketika obat ini digunakan dengan obat antidiabetes oral selain sulfonilurea atau insulin.

Tanda – tanda peringatan kadar gula darah yang rendah mungkin datang tiba-tiba. Tanda – tanda tersebut dapat mencakup: keringat dingin, kulit pucat dingin, sakit kepala, detak jantung cepat, mual atau sangat lapar, perubahan pandangan, merasa mengantuk atau lemah, merasa gugup, cemas atau bingung, kesulitan berkonsentrasi atau gemetar. Dokter Anda akan memberitahu Anda bagaimana cara mengobati kadar gula darah yang rendah dan apa yang dilakukan jika Anda melihat tanda – tanda peringatan tersebut. Kadar gula darah yang rendah lebih mungkin terjadi jika Anda juga mengonsumsi sulfonilurea atau insulin. Dokter Anda mungkin mengurangi dosis obat – obatan tersebut sebelum Anda mulai menggunakan obat ini.

- gangguan pencernaan
- radang perut (gastritis) – tanda – tanda termasuk sakit perut, mual atau muntah
- refluks atau rasa panas di perut - juga disebut *gastro-esophageal reflux disease* (GERD)
- nyeri perut
- perut kembung
- konstipasi
- sendawa
- batu empedu
- pusing
- kelelahan
- penurunan berat badan
- kurang nafsu makan
- kentut (flatulensi)
- peningkatan enzim pankreas (seperti lipase dan amilase).

Tidak umum (mungkin memengaruhi hingga 1 dari 100 orang)

- perubahan rasa makanan atau minuman
- denyut nadi cepat
- reaksi di tempat penyuntikan - seperti memar, nyeri, iritasi, gatal dan ruam
- reaksi alergi seperti ruam, gatal atau bentol
- penundaan pengosongan lambung

Pelaporan efek samping

Jika Anda mengalami efek samping apapun, bicarakan dengan dokter, apoteker atau perawat Anda. Hal tersebut termasuk efek samping yang mungkin tidak tercantum dalam brosur ini. Dengan melaporkan efek samping Anda dapat membantu menyediakan lebih banyak informasi keamanan obat ini.

5. Bagaimana cara menyimpan Ozempic®

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan obat ini setelah tanggal kadaluwarsa yang tertera di label pena dan karton setelah 'Expiry'. Tanggal kadaluwarsa mengacu di hari terakhir dari bulan tersebut.

Sebelum dibuka:

STF JUNE 2023

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Simpan di lemari pendingin (2°C - 8°C). Jangan dibekukan. Jauhkan dari elemen pendingin. Pasang tutup pena untuk melindunginya dari cahaya.

Selama penggunaan:

- Anda dapat menyimpan pena selama 6 minggu jika disimpan di suhu di bawah 30°C atau dalam lemari pendingin (2°C - 8°C) jauh dari elemen pendingin. Jangan membekukan Ozempic® dan jangan menggunakannya jika sudah membeku.
- Ketika Anda tidak menggunakan pena, pasang tutup pena untuk melindunginya dari cahaya.

Jangan menggunakan obat ini jika Anda melihat bahwa larutan obat ini tidak jernih dan tidak berwarna atau hampir tidak berwarna.

Jangan membuang obat – obatan melalui air limbah atau sampah rumah tangga. Tanyakan kepada apoteker Anda bagaimana cara membuang obat – obatan yang Anda tidak lagi gunakan. Langkah-langkah tersebut akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lain

Apa kandungan Ozempic®

- Zat aktifnya adalah semaglutide. Larutan injeksi satu ml mengandung 1,34 mg semaglutide. Satu pena yang sudah terisi mengandung 2 mg semaglutide dalam 1,5 ml larutan.
- Zat lainnya adalah: dinatrium fosfat dihidrat, propilen glikol, fenol, air untuk injeksi, natrium hidroksida / asam hidroklorida (untuk penyesuaian pH). Lihat juga bagian 2 'Kandungan natrium'.

Seperti apa Ozempic® dan isiemasannya

Ozempic® adalah larutan injeksi jernih dan tidak berwarna atau hampir tidak berwarna dalam pena yang sudah terisi.

Setiap pena berisi 1,5 ml larutan, menyuntikkan dosis 0,25 atau 0,5 mg.

Larutan injeksi Ozempic® 0,25 mg; 0,5 mg tersedia dalam kemasan berikut:

1 pena dan 6 jarum sekali pakai NovoFine® Plus.

HARUS DENGAN RESEP DOKTER

Reg. No.: DKIXXXXXXXXXXXXX

Diproduksi oleh:

Novo Nordisk A/S
Brennum Park
DK-3400 Hillerød
Denmark

Dirilis oleh:

Novo Nordisk A/S
Novo Alle

DK-2880 Bagsværd
Denmark

Didaftarkan oleh:

PT Beta Pharmacon
Indonesia

Didistribusikan oleh:

PT Anugrah Argon Medica
Indonesia

Berdasarkan persetujuan tanggal:

Ozempic®, *NovoFine®* dan *NovoTwist®* adalah merek dagang yang dimiliki oleh Novo Nordisk A/S, Denmark.

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Novo Nordisk A/S

Ozempic®

1,34 mg/ml

0,25 mg; 0,5 mg/dosis

larutan injeksi dalam pena yang sudah terisi

semaglutide

Instruksi bagaimana cara menggunakan Ozempic® 0,25 mg; 0,5 mg/dosis larutan injeksi dalam pena yang sudah terisi

Bacalah instruksi ini dengan teliti sebelum menggunakan pena yang sudah terisi Ozempic® Anda.

Bicarakan dengan dokter, perawat atau apoteker Anda tentang bagaimana menyuntikkan Ozempic® dengan benar.

Mulai dengan memeriksa pena Anda **untuk memastikan pena berisi Ozempic® 0,25 mg; 0,5 mg/dosis** kemudian lihat gambar di bawah ini untuk mengenal bagian - bagian yang berbeda dari pena dan jarum Anda.

Jika Anda buta atau memiliki penglihatan yang buruk dan tidak dapat membaca penghitung dosis di pena, jangan menggunakan pena ini tanpa bantuan. Dapatkan bantuan dari seseorang dengan penglihatan yang baik yang mengetahui bagaimana menggunakan pena yang sudah terisi Ozempic®.

Pena Anda adalah pena *dial-a-dose* yang sudah terisi. Pena mengandung 2 mg semaglutide, dan Anda hanya dapat memilih dosis 0,25 mg atau 0,5 mg.

Satu pena yang belum digunakan mengandung:

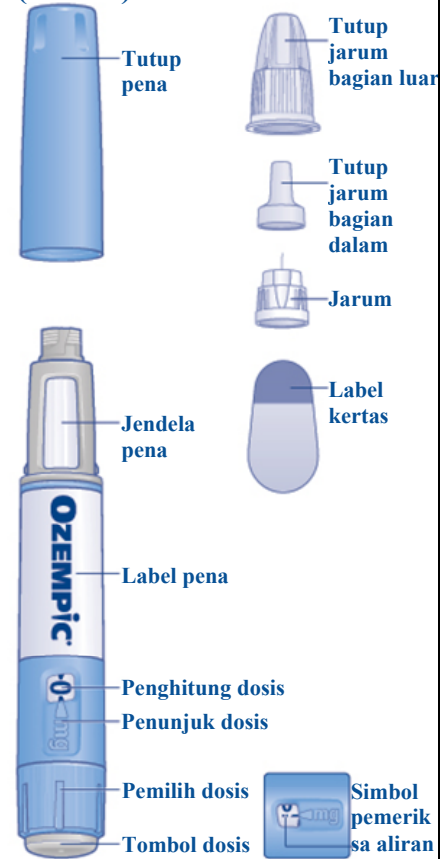
- 4 dosis 0,25 mg (dosis awal) dan 2 dosis 0,5 mg
- **atau** 4 dosis 0,5 mg

Gunakan tabel di dalam karton untuk melacak berapa banyak penyuntikan yang telah Anda lakukan dan kapan Anda melakukan penyuntikan.

Pena Anda didesain untuk digunakan dengan jarum sekali pakai NovoFine® dan NovoTwist® dengan panjang hingga 8 mm.

Jarum NovoFine® Plus sudah termasuk dalam kemasan.

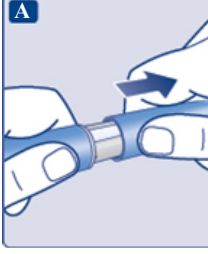
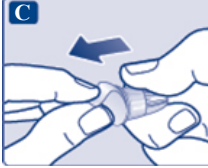
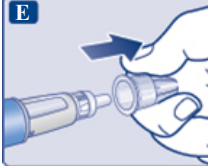
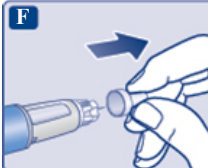
Pena yang sudah terisi Ozempic® dan jarum (contoh)



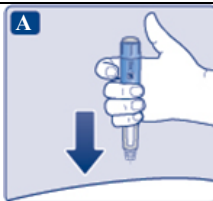
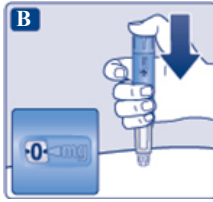
Informasi penting

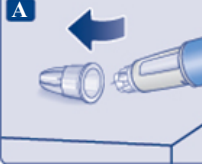
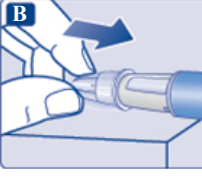
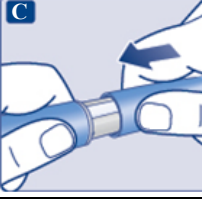
Berikan perhatian khusus di catatan ini, karena penting untuk penggunaan pena yang aman.

1. Mempersiapkan pena Anda dengan jarum baru

• Periksa nama dan label warna pena Anda, untuk memastikan bahwa pena berisi Ozempic® 0,25 mg; 0.5 mg/dosis. Hal tersebut terutama penting jika Anda mengonsumsi lebih dari satu jenis obat suntik. Menggunakan obat yang salah dapat berbahaya bagi kesehatan Anda. • Cabut tutup pena.		
• Periksa bahwa larutan dalam pena Anda jernih dan tidak berwarna. Lihat melalui jendela pena. Jika larutan terlihat keruh atau berwarna, jangan menggunakan pena.		
• Ambil jarum baru Periksa label kertas dan tutup jarum bagian luar untuk kerusakan yang dapat memengaruhi sterilitas. Jika terlihat kerusakan apapun gunakan jarum baru. • Lepaskan label kertasnya.		
Pastikan untuk memasang jarum dengan benar. • Tekan jarum lurus ke pena. • Putar hingga terpasang erat.		
Jarum tertutup oleh 2 tutup. Anda harus melepaskan kedua tutup. Jika Anda lupa melepaskan kedua tutup, Anda tidak akan menyuntikkan larutan apapun. • Cabut tutup jarum bagian luar dan simpan untuk nanti. Anda akan memerlukannya setelah penyuntikan, untuk melepaskan jarum dari pena dengan aman.		
• Cabut tutup jarum bagian dalam dan buang. Jika Anda mencoba untuk memasangnya kembali, Anda mungkin tertusuk jarum secara tidak sengaja. Setetes larutan mungkin muncul di ujung jarum. Hal tersebut normal, tetapi Anda tetap harus memeriksa aliran, jika Anda menggunakan pena baru untuk pertama kalinya. Lihat langkah 2 'Memeriksa aliran dengan setiap pena baru'. Jangan memasang jarum baru untuk pena Anda hingga Anda siap untuk melakukan penyuntikan Anda.		
 Selalu gunakan jarum baru untuk setiap penyuntikan. Hal tersebut mungkin mencegah jarum tersumbat, kontaminasi, infeksi dan dosis		

yang tidak akurat.	
⚠ Jangan pernah menggunakan jarum yang bengkok atau rusak.	
2. Memeriksa aliran dengan setiap pena baru	
- Jika pena Anda telah digunakan, lanjutkan ke langkah 3 'Memilih dosis Anda'. Periksa aliran hanya sebelum penyuntikan pertama Anda dengan setiap pena baru. - Putar pemilih dosis ke simbol pemeriksa aliran (●—) tepat setelah '0'. Pastikan simbol pemeriksa aliran sejajar dengan penunjuk.	 Simbol pemeriksa aliran dipilih
Pegang pena dengan jarum mengarah ke atas. Tekan dan tahan tombol dosis hingga penghitung dosis kembali ke '0'. '0' harus sejajar dengan penunjuk dosis. Setetes larutan seharusnya muncul di ujung jarum.	
Sedikit tetesan mungkin tetap ada di ujung jarum, tetapi tidak akan disuntikkan. Jika tetesan tidak muncul, ulangi langkah 2 'Memeriksa aliran dengan setiap pena baru' hingga 6 kali. Jika masih tidak ada tetesan, ganti jarum dan ulangi langkah 2 'Memeriksa aliran dengan setiap pena baru' sekali lagi. Buang pena dan gunakan pena baru jika tetesan larutan masih tidak muncul.	
⚠ Selalu pastikan bahwa tetesan muncul di ujung jarum sebelum Anda menggunakan pena baru untuk pertama kalinya. Hal tersebut memastikan bahwa larutan mengalir. Jika tetesan tidak muncul, Anda tidak akan menyuntikkan obat apapun meskipun penghitung dosis mungkin bergerak. Hal tersebut mungkin menunjukkan jarum tersumbat atau rusak. Jika Anda tidak memeriksa aliran sebelum penyuntikan pertama Anda dengan masing-masing pena baru, Anda mungkin tidak mendapatkan dosis yang diresepkan dan efek yang diinginkan dari Ozempic®.	
3. Memilih dosis Anda	
Putar pemilih dosis hingga penghitung dosis menunjukkan dosis yang sudah diresepkan (0,25 mg atau 0,5 mg). - Jika Anda salah memilih dosis, Anda dapat memutar pemilih dosis ke depan atau belakang ke dosis yang benar. - Pena dapat memilih hingga maksimum 0,5 mg.	 Contoh 0,25 mg dipilih
Pemilih dosis mengubah dosis. Hanya penghitung dosis dan penunjuk dosis yang akan menunjukkan berapa mg yang Anda pilih per dosis. Anda dapat memilih hingga 0,5 mg per dosis. Ketika pena Anda mengandung kurang dari	

0,5 mg, penghitung dosis berhenti sebelum 0,5 mg ditunjukkan. Pemilih dosis berbunyi klik berbeda ketika diputar ke depan, belakang atau melewati jumlah mg yang tersisa. Jangan menghitung klik pena.	
⚠ Selalu gunakan penghitung dosis dan penunjuk dosis untuk melihat berapa mg yang sudah Anda pilih sebelum menyuntikkan obat ini. Jangan menghitung klik pena. Hanya dosis 0,25 mg atau 0,5 mg yang harus dipilih oleh pemilih dosis. Dosis yang dipilih harus tepat sejajar dengan penunjuk dosis untuk memastikan bahwa Anda mendapatkan dosis yang benar.	
Berapa jumlah larutan yang tersisa	
Untuk melihat berapa jumlah larutan yang tersisa, Gunakan penghitung dosis: Putar pemilih dosis hingga penghitung dosis berhenti. Jika penghitung dosis menunjukkan 0,5, setidaknya 0,5 mg yang tersisa dalam pena Anda. - Jika penghitung dosis berhenti sebelum 0,5 mg, tidak ada cukup larutan yang tersisa untuk dosis penuh 0,5 mg.	 A Contoh Penghitung dosis berhenti: tersisa 0,25 mg
⚠ Jika tidak ada cukup larutan yang tersisa dalam pena Anda untuk dosis penuh, jangan menggunakannya. Gunakan pena Ozempic® yang baru.	
4. Menyuntikkan dosis Anda	
Masukkan jarum ke dalam kulit Anda sebagaimana yang ditunjukkan oleh dokter atau perawat Anda. Pastikan Anda dapat melihat penghitung dosis. Jangan menutupinya dengan jari-jari Anda. Hal tersebut dapat mengganggu penyuntikan.	 B
Tekan dan tahan tombol dosis. Lihat ketika penghitung dosis kembali ke '0'. '0' harus sejajar dengan penunjuk dosis. Anda kemudian mungkin mendengar atau merasakan klik. Terus tekan tombol dosis ketika jarum di dalam kulit Anda.	 C Hitung perlahan-lahan 1-2-3-4-5-6
Hitung perlahan-lahan hingga 6, ketika tombol dosis ditekan. - Jika jarum dicabut lebih cepat, Anda mungkin melihat aliran larutan yang berasal dari ujung jarum. Jika demikian, dosis penuh tidak akan didapatkan.	 D Hitung perlahan-lahan 1-2-3-4-5-6

• Lepaskan jarum dari kulit Anda. Anda dapat melepaskan tombol dosis. Jika darah muncul di lokasi penyuntikan, tekan perlahan.	
Anda mungkin melihat tetesan larutan di ujung jarum setelah penyuntikan. Hal tersebut normal dan tidak memengaruhi dosis Anda.	
⚠ Selalu perhatikan penghitung dosis untuk mengetahui berapa jumlah mg yang Anda suntikkan. Tahan tombol dosis ke bawah hingga penghitung dosis kembali ke '0'. Bagaimana mengidentifikasi jarum yang tersumbat atau rusak – Jika '0' tidak muncul di penghitung dosis setelah Anda terus menerus menekan tombol dosis, maka Anda mungkin sudah menggunakan jarum yang tersumbat atau rusak. – Dalam hal tersebut, Anda belum menerima obat apapun - meskipun penghitung dosis sudah bergerak dari dosis awal yang sudah diatur. Bagaimana menangani jarum yang tersumbat Ganti jarum seperti yang dijelaskan di langkah 5 'Setelah penyuntikan Anda' dan ulangi semua langkah dimulai dengan langkah 1 'Memersiapkan pena Anda dengan jarum baru'. Pastikan Anda memilih dosis penuh yang Anda perlukan. Jangan pernah menyentuh penghitung dosis ketika Anda menyuntikkan. Hal tersebut dapat mengganggu penyuntikan.	
5. Setelah penyuntikan Anda	
Selalu buang jarum setelah setiap penyuntikan untuk memastikan penyuntikan yang nyaman dan mencegah jarum tersumbat. Jika jarum tersumbat, Anda tidak akan menyuntikkan obat apapun. • Arahkan ujung jarum ke tutup jarum bagian luar di permukaan yang datar tanpa menyentuh jarum atau tutup jarum bagian luar.	
• Setelah jarum tertutup, dorong pelan-pelan tutup jarum bagian luar sepenuhnya. • Lepaskan jarum dan buang dengan hati-hati seperti yang diinstruksikan oleh dokter, perawat, apoteker atau pihak berwenang setempat Anda.	
• Pasang tutup pena di pena Anda setelah setiap penggunaan untuk melindungi larutan dari cahaya.	
Ketika pena kosong, buang pena tanpa jarum seperti yang diinstruksikan oleh dokter,	

perawat, apoteker atau pihak berwenang setempat Anda.	
⚠	Jangan pernah mencoba untuk memasang kembali tutup jarum bagian dalam. Anda mungkin tertusuk jarum.
⚠	Selalu lepaskan jarum dari pena Anda segera setelah setiap penyuntikan. Hal tersebut mungkin mencegah jarum tersumbat, kontaminasi, infeksi, kebocoran larutan dan dosis yang tidak akurat.
⚠	Informasi penting lebih lanjut
- Selalu simpan pena dan jarum dari pandangan dan jangkauan orang lain, terutama anak-anak. Jangan pernah berbagi pena atau jarum Anda dengan orang lain. - Perawat harus sangat berhati-hati ketika menangani jarum bekas untuk mencegah cedera tertusuk jarum dan infeksi silang.	
Pemeliharaan pena Anda	
Perlakukan pena Anda dengan hati-hati. Penanganan yang kasar atau penyalahgunaan dapat menyebabkan dosis yang tidak akurat. Jika hal tersebut terjadi, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini.	
Jangan meninggalkan pena di dalam mobil atau tempat lain dimana pena dapat menjadi terlalu panas atau terlalu dingin. Jangan menyuntikkan Ozempic® yang sudah membeku. Jika Anda melakukannya, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini. Jangan menyuntikkan Ozempic® yang sudah terpapar sinar matahari langsung. Jika Anda melakukannya, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini. Jangan memaparkan pena Anda ke debu, kotoran atau larutan. Jangan mencuci, merendam atau melumasi pena Anda. Pena mungkin dibersihkan dengan deterjen ringan di kain yang lembab. Jangan menjatuhkan pena Anda atau membenturkan di permukaan yang keras. Jika Anda menjatuhkannya atau menduga ada masalah, pasang jarum baru dan periksa aliran sebelum Anda menyuntikkan. Jangan mencoba untuk mengisi ulang pena Anda. Setelah habis, pena harus dibuang. Jangan mencoba untuk memperbaiki pena Anda atau memisahkan bagian – bagiannya.	

1. Name of medicinal product**Ozempic®**

1.34 mg/ml

1 mg/dose

Solution for injection in pre-filled pen

2. Qualitative and quantitative composition

One ml of solution contains 1.34 mg of semaglutide*. One pre-filled pen contains 4 mg semaglutide* in 3 ml solution. Each dose contains 1 mg of semaglutide in 0.74 ml solution.

*Human glucagon-like peptide-1 (GLP-1) analogue produced in *Saccharomyces cerevisiae* cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection.

Clear and colourless or almost colourless, isotonic solution; pH=7.4.

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 in addition to metformin, metformin and sulphonylurea, metformin and basal insulin, or sodium-glucose cotransporter 2 (SGLT2) inhibitor.

For trial results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1.

4.2 Posology and method of administrationPosology

The starting dose is 0.25 mg semaglutide 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.

Semaglutide 0.25 mg is not a maintenance dose. Weekly doses higher than 1 mg are not recommended.

When Ozempic® is added to existing metformin therapy or to a SGLT2 inhibitor, the current dose of metformin or SGLT2 inhibitor can be continued unchanged.

When Ozempic® is added to existing therapy of sulphonylurea or insulin, a reduction in the dose of sulphonylurea or insulin should be considered to reduce the risk of hypoglycaemia (see sections 4.4 and 4.8).

Self-monitoring of blood glucose is not needed in order to adjust the dose of Ozempic®. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea and insulin, particularly when Ozempic® is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.

Missed dose

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.

Changing the dosing day

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.

Special populations

Elderly

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

Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease (see section 5.2).

Hepatic impairment

No dose adjustment is required for patients with 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 (see section 5.2).

Paediatric population

The safety and efficacy of semaglutide in children and adolescents below 18 years have not yet been established. No data are available.

Method of administration

Subcutaneous use.

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.

Ozempic® is to be administered once weekly at any time of the day, with or without meals.

For further information on administration, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

General

Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Semaglutide is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients whom had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started (see section 4.2).

There is no experience in patients with congestive heart failure NYHA class IV and semaglutide is therefore not recommended in these patients.

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 (see section 4.8).

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, semaglutide should be discontinued; if confirmed, semaglutide should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Hypoglycaemia

Patients treated with semaglutide 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 semaglutide (see section 4.8).

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). Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin. These patients should be monitored closely and treated according to clinical guidelines. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Semaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption.

Paracetamol

Semaglutide delays the rate of gastric emptying as assessed by paracetamol pharmacokinetics during a standardised meal test. Paracetamol $AUC_{0-60\text{min}}$ and C_{max} were decreased by 27% and 23%, respectively, following concomitant use of semaglutide 1 mg. The total paracetamol exposure (AUC_{0-5h}) was not affected. No dose adjustment of paracetamol is necessary when administered with semaglutide.

Oral contraceptives

Semaglutide is not anticipated to decrease the effect 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 the 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 (INR) were not affected in a clinically relevant manner. However, upon initiation of semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of INR is recommended.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential are recommended to use contraception when treated with semaglutide.

Pregnancy

Studies in animals have shown reproductive toxicity (see section 5.3). There are limited data from the use of semaglutide in pregnant women. Therefore, semaglutide should not be used during pregnancy. 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 5.2).

Breast-feeding

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

Fertility

The effect of semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats. 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 (see section 5.3).

4.7 Effects on ability to drive and use machines

Semaglutide 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 (see section 4.4).

4.8 Undesirable effects

Summary of safety profile

In 8 phase 3a trials 4,792 patients were exposed to semaglutide. The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea (very common), diarrhoea (very common) and vomiting (common). In general, these reactions were mild or moderate in severity and of short duration.

Tabulated list of adverse reactions

Table 1 lists adverse reactions identified in all phase 3 trials (including the long-term cardiovascular outcomes trial) and post-marketing reports in patients with type 2 diabetes mellitus (further described in section 5.1). The frequencies of the adverse reactions (except diabetic retinopathy complications, see footnote in Table 1) are based on a pool of the phase 3a trials excluding the cardiovascular outcomes trial (see text below the table for additional details).

The reactions are listed below by system organ class and absolute frequency. Frequencies are defined as: very common: ($\geq 1/10$); common: ($\geq 1/100$ to $< 1/10$); uncommon: ($\geq 1/1\ 000$ to $< 1/100$); rare: ($\geq 1/10\ 000$ to $< 1/1\ 000$); very rare: ($< 1/10\ 000$) and not known: cannot be estimated from available data. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 Frequency of adverse reactions of semaglutide

MedDRA system organ class	Very common	Common	Uncommon	Rare	Not known
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 oral antidiabetics (OAD) 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 Delayed gastric emptying		
Hepatobiliary disorders		Cholelithiasis			
Skin and subcutaneous tissue disorders					Angioedema ^d
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: retinal photocoagulation, treatment with intravitreal agents, vitreous haemorrhage, diabetes-related blindness (uncommon). Frequency based on cardiovascular outcomes trial.

^{c)} Grouped term covering also adverse events related to hypersensitivity such as rash and urticaria.

^{d)} From post-marketing reports.

2-year cardiovascular outcomes and safety trial

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

Description of selected adverse reactions

Hypoglycaemia

Severe hypoglycaemia was primarily observed when semaglutide 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 episodes (0.1% of subjects, 0.001 events/patient year) were observed with semaglutide in combination with oral antidiabetics other than sulfonylureas.

American Diabetes Association (ADA) classified hypoglycaemia occurred in 11.3% (0.3 events/patient year) of patients when semaglutide 1 mg was added to SGLT2 inhibitor in SUSTAIN 9 compared to 2.0% (0.04 events/patient year) of placebo-treated patients. Severe hypoglycaemia was reported in 0.7% (0.01 events/patient year) and 0% of patients, respectively.

Gastrointestinal adverse reactions

Nausea occurred in 17% and 19.9% of patients when treated with semaglutide 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% of patients. 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.

In concomitant use with an SGLT2 inhibitor in SUSTAIN 9, constipation and gastro-oesophageal reflux disease occurred in 6.7% and 4% respectively of patients treated with semaglutide 1 mg compared to no events for placebo-treated patients. The prevalence of these events did not decrease over time.

Acute pancreatitis

The frequency of adjudication-confirmed acute pancreatitis reported in phase 3a clinical trials was 0.3% for semaglutide and 0.2% for the comparator, respectively. In the 2-year cardiovascular outcomes trial the frequency of acute pancreatitis confirmed by adjudication was 0.5% for semaglutide and 0.6% for placebo (see section 4.4).

Diabetic retinopathy complications

A 2-year clinical trial investigated 3,297 patients with type 2 diabetes, with high cardiovascular risk, long duration of diabetes and poorly controlled blood glucose. In this trial, adjudicated events of diabetic retinopathy complications occurred in more patients treated with semaglutide (3%) compared to placebo (1.8%). This was observed in insulin-treated patients with known diabetic retinopathy. The treatment difference appeared early and persisted throughout the trial. Systematic evaluation of diabetic retinopathy complication was only performed in the cardiovascular outcomes trial. In clinical trials up to 1 year involving 4,807 patients with type 2 diabetes, adverse events related to diabetic retinopathy were reported in similar proportions of subjects treated with semaglutide (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, vs. 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. 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 (1-3%) 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 Ozempic®. In a long-term trial in subjects with cardiovascular risk factors, 16% of Ozempic®-treated subjects had an increase in heart rate of >10 bpm compared to 11% of subjects on placebo after 2 years of treatment.

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 reaction was nausea. All patients recovered without complications.

There is no specific antidote for overdose with semaglutide. 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 semaglutide of approximately 1 week (see section 5.2).

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 selectively 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.

Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. 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. In addition, semaglutide reduces the preference for high fat foods.

GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. 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) and relative reduction compared to placebo (%) for fasting glucose (1.6 mmol/l; 22% reduction), 2 hour postprandial glucose (4.1 mmol/l; 37% reduction), mean 24 hour glucose concentration (1.7 mmol/l; 22% reduction) and postprandial glucose excursions over 3 meals (0.6–1.1 mmol/l) compared with placebo. Semaglutide lowered fasting glucose after the first dose.

Beta-cell function and insulin secretion

Semaglutide improves beta-cell function. Compared to placebo, semaglutide improved first- and second-phase insulin response with a 3- and 2-fold increase, respectively, and increased maximal beta-cell secretory capacity 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.

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.

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 very low-density lipoproteins (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 dose levels (up to 1.5 mg at steady state).

Clinical efficacy and safety

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 semaglutide 0.5 mg and 1 mg once weekly were evaluated in six randomised controlled phase 3a trials that included 7,215 patients with type 2 diabetes mellitus (4,107 treated with semaglutide). Five trials (SUSTAIN 1–5) had the glycaemic efficacy assessment as the primary objective, while one trial (SUSTAIN 6) had cardiovascular outcome as the primary objective.

In addition, a phase 3b trial (SUSTAIN 7) including 1,201 patients was conducted to compare the efficacy and safety of semaglutide 0.5 mg and 1 mg once weekly to dulaglutide 0.75 mg and 1.5 mg once weekly, respectively. A phase 3b trial (SUSTAIN 9), was conducted to investigate the efficacy and safety of semaglutide as add-on to SGLT2 inhibitor treatment.

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

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

In addition, a phase 3b trial (SUSTAIN 11), was conducted to investigate the effect of semaglutide vs. insulin aspart, both as add-on to metformin and optimised insulin glargine (U100).

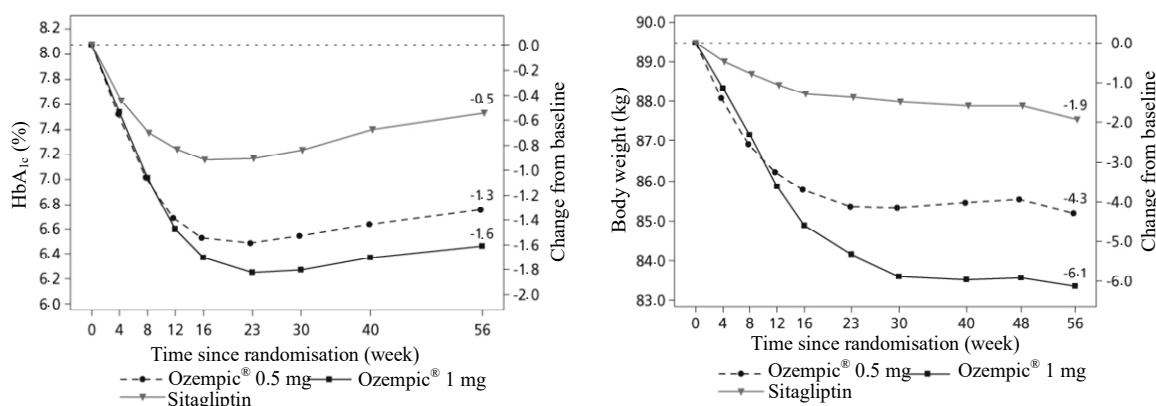
Detailed information is provided below.

SUSTAIN 2 – Semaglutide vs. sitagliptin both in combination with 1–2 oral antidiabetic medicinal products (metformin and/or thiazolidinediones)

In a 56-week active-controlled double-blind trial, 1,231 patients were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or sitagliptin 100 mg once daily, all in combination with metformin (94%) and/or thiazolidinediones (6%).

Table 2 SUSTAIN 2: Results at week 56

	Semaglutide 0.5 mg	Semaglutide 1 mg	Sitagliptin 100 mg
Intent-to-Treat (ITT) Population (N)	409	409	407
HbA_{1c} (%)			
Baseline (mean)	8.0	8.0	8.2
Change from baseline at week 56	-1.3	-1.6	-0.5
Difference from sitagliptin [95% CI]	-0.8 [-0.9, -0.6] ^a	-1.1 [-1.2, -0.9] ^a	-
Patients (%) achieving HbA_{1c} <7%	69	78	36
FPG (mmol/l)			
Baseline (mean)	9.3	9.3	9.6
Change from baseline at week 56	-2.1	-2.6	-1.1
Body weight (kg)			
Baseline (mean)	89.9	89.2	89.3
Change from baseline at week 56	-4.3	-6.1	-1.9
Difference from sitagliptin [95% CI]	-2.3 [-3.1, -1.6] ^a	-4.2 [-4.9, -3.5] ^a	-

^ap <0.0001 (2-sided) for superiority

Figure 1 Mean change in HbA_{1c} (%) and body weight (kg) from baseline to week 56

SUSTAIN 7 – Semaglutide vs. dulaglutide both in combination with metformin

In a 40-week, open-label trial, 1,201 patients on metformin were randomised 1:1:1:1 to once weekly semaglutide 0.5 mg, dulaglutide 0.75 mg, semaglutide 1 mg or dulaglutide 1.5 mg, respectively.

The trial compared 0.5 mg of semaglutide to 0.75 mg of dulaglutide and 1 mg of semaglutide to 1.5 mg of dulaglutide.

Gastrointestinal disorders were the most frequent adverse events, and occurred in similar proportion of patients receiving semaglutide 0.5 mg (129 patients [43%]), semaglutide 1 mg (133 [44%]), and dulaglutide 1.5 mg (143 [48%]); fewer patients had gastrointestinal disorders with dulaglutide 0.75 mg (100 [33%]).

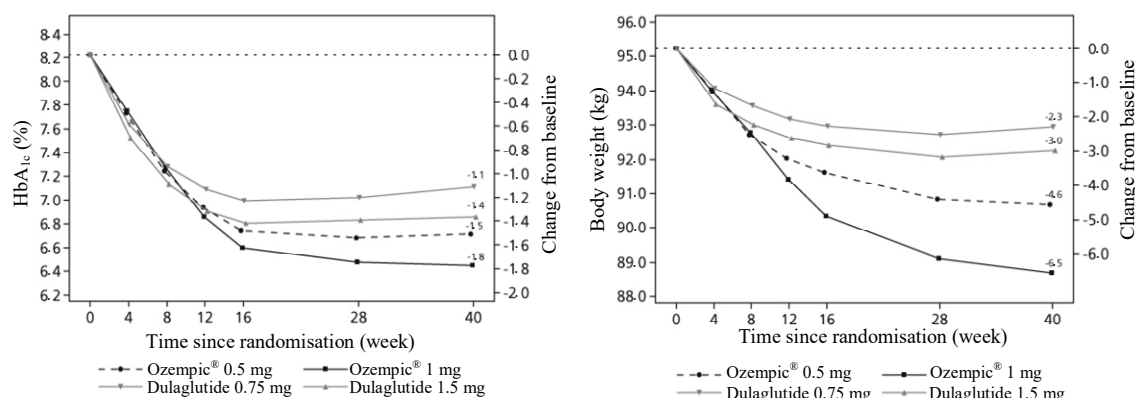
At week 40, the increase in pulse rate for semaglutide (0.5 mg and 1 mg) and dulaglutide (0.75 mg and 1.5 mg) was 2.4, 4.0, and 1.6, 2.1, beats/min, respectively.

Table 3 SUSTAIN 7: Results at week 40

	Semaglutide 0.5 mg	Semaglutide 1 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Intent-to-Treat (ITT) Population (N)	301	300	299	299
HbA_{1c} (%)				
Baseline (mean)	8.3	8.2	8.2	8.2
Change from baseline at week 40	-1.5	-1.8	-1.1	-1.4
Difference from dulaglutide [95% CI]	-0.4 ^b [-0.6, -0.2] ^a	-0.4 ^c [-0.6, -0.3] ^a	-	-
Patients (%) achieving HbA_{1c} <7%	68	79	52	67
FPG (mmol/l)				
Baseline (mean)	9.8	9.8	9.7	9.6
Change from baseline at week 40	-2.2	-2.8	-1.9	-2.2
Body weight (kg)				
Baseline (mean)	96.4	95.5	95.6	93.4
Change from baseline at week 40	-4.6	-6.5	-2.3	-3.0
Difference from dulaglutide [95% CI]	-2.3 ^b [-3.0, -1.5] ^a	-3.6 ^c [-4.3, -2.8] ^a	-	-

^ap <0.0001 (2-sided) for superiority

^bSemaglutide 0.5 mg vs. dulaglutide 0.75 mg

^cSemaglutide 1 mg vs. dulaglutide 1.5 mg

Figure 2 Mean change in HbA_{1c} (%) and body weight (kg) from baseline to week 40

SUSTAIN 3 – Semaglutide vs. exenatide ER both in combination with metformin or metformin with sulfonylurea

In a 56-week open-label trial, 813 patients on metformin alone (49%), metformin with sulfonylurea (45%) or other (6%) were randomised to semaglutide 1 mg or exenatide ER 2 mg once weekly.

Table 4 SUSTAIN 3: Results at week 56

	Semaglutide 1 mg	Exenatide ER 2 mg
Intent-to-Treat (ITT) Population (N)	404	405
HbA_{1c} (%)		
Baseline (mean)	8.4	8.3
Change from baseline at week 56	-1.5	-0.9
Difference from exenatide [95% CI]	-0.6 [-0.8, -0.4] ^a	-
Patients (%) achieving HbA_{1c} <7%	67	40
FPG (mmol/l)		
Baseline (mean)	10.6	10.4
Change from baseline at week 56	-2.8	-2.0
Body weight (kg)		
Baseline (mean)	96.2	95.4
Change from baseline at week 56	-5.6	-1.9
Difference from exenatide [95% CI]	-3.8 [-4.6, -3.0] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 4 – Semaglutide vs. insulin glargine both in combination with 1–2 oral antidiabetic medicinal products (metformin or metformin and sulfonylurea)

In a 30-week open-label comparator trial 1,089 patients were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly, or insulin glargine once-daily on a background of metformin (48%) or metformin and sulfonylurea (51%).

Table 5 SUSTAIN 4: Results at week 30

	Semaglutide 0.5 mg	Semaglutide 1 mg	Insulin Glargine
Intent-to-Treat (ITT) Population (N)	362	360	360
HbA_{1c} (%)			
Baseline (mean)	8.1	8.2	8.1
Change from baseline at week 30	-1.2	-1.6	-0.8
Difference from insulin glargine [95% CI]	-0.4 [-0.5, -0.2] ^a	-0.8 [-1.0, -0.7] ^a	-
Patients (%) achieving HbA_{1c} <7%	57	73	38
FPG (mmol/l)			
Baseline (mean)	9.6	9.9	9.7
Change from baseline at week 30	-2.0	-2.7	-2.1
Body weight (kg)			
Baseline (mean)	93.7	94.0	92.6
Change from baseline at week 30	-3.5	-5.2	+1.2
Difference from insulin glargine [95% CI]	-4.6 [-5.3, -4.0] ^a	-6.34 [-7.0, -5.7] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 5 – Semaglutide vs. placebo both in combination with basal insulin

In a 30-week double-blind placebo-controlled trial, 397 patients inadequately controlled with basal insulin with or without metformin were randomised to semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or placebo.

Table 6 SUSTAIN 5: Results at week 30

	Semaglutide 0.5 mg	Semaglutide 1 mg	Placebo
Intent-to-Treat (ITT) Population (N)	132	131	133
HbA_{1c} (%)			
Baseline (mean)	8.4	8.3	8.4
Change from baseline at week 30	-1.4	-1.8	-0.1
Difference from placebo [95% CI]	-1.4 [-1.6, -1.1] ^a	-1.8 [-2.0, -1.5] ^a	-
Patients (%) achieving HbA_{1c} <7%	61	79	11
FPG (mmol/l)			
Baseline (mean)	8.9	8.5	8.6
Change from baseline at week 30	-1.6	-2.4	-0.5
Body weight (kg)			
Baseline (mean)	92.7	92.5	89.9
Change from baseline at week 30	-3.7	-6.4	-1.4
Difference from placebo [95% CI]	-2.3 [-3.3, -1.3] ^a	-5.1 [-6.1, -4.0] ^a	-

^ap <0.0001 (2-sided) for superiority

SUSTAIN 9 – Semaglutide vs. placebo as add-on to SGLT2 inhibitor ± metformin or sulfonylurea

In a 30-week double-blind placebo-controlled trial, 302 patients inadequately controlled with SGLT2 inhibitor with or without metformin or sulfonylurea were randomised to semaglutide 1 mg once weekly or placebo.

Table 7 SUSTAIN 9: Results at week 30

	Semaglutide 1 mg	Placebo
Intent-to-Treat (ITT) Population (N)	151	151
HbA_{1c} (%)		
Baseline (mean)	8.0	8.1
Change from baseline at week 30	-1.5	-0.1
Difference from placebo [95% CI]	-1.4 [-1.6, -1.2] ^a	-
Patients (%) achieving HbA_{1c} <7%	78.7	18.7
FPG (mmol/L)		
Baseline (mean)	9.1	8.9
Change from baseline at week 30	-2.2	0.0
Body weight (kg)		
Baseline (mean)	89.6	93.8
Change from baseline at week 30	-4.7	-0.9
Difference from placebo [95% CI]	-3.8 [-4.7, -2.9] ^a	-

^ap < 0.0001 (2-sided) for superiority, adjusted regarding multiplicity based on hierarchical testing of the HbA_{1c} value and body weight

SUSTAIN 11 - Semaglutide vs. insulin aspart as add-on to insulin glargine + metformin

In a 52-week open-label trial, 1 748 subjects with inadequately controlled T2D after a 12-week run-in period on insulin glargine and metformin were randomised to 1:1 to receive either semaglutide once-weekly (0.5 mg or 1.0 mg) or insulin aspart three times daily. The

included population had a mean diabetes duration of 13.4 years and a mean HbA_{1c} of 8.6%, with a target HbA_{1c} of 6.5-7.5%.

Treatment with semaglutide resulted in reduction in HbA_{1c} at week 52 (-1.5% for semaglutide vs. -1.2% for insulin aspart).

The number of severe hypoglycaemic episodes in both treatment arms was low (4 episodes with semaglutide vs. 7 episodes with insulin aspart).

Mean baseline body weight decreased with semaglutide (-4.1 kg) and increased with insulin aspart (+2.8 kg) and the estimated treatment difference was -6.99 kg (95%CI -7.41 to -6.57) at week 52.

Combination with sulfonylurea monotherapy

In SUSTAIN 6 (see subsection 'Cardiovascular disease') 123 patients were on sulfonylurea monotherapy at baseline. HbA_{1c} at baseline was 8.2%, 8.4% and 8.4% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively. At week 30, the change in HbA_{1c} was -1.6%, -1.5% and 0.1% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively.

Combination with premix insulin ± 1–2 OADs

In SUSTAIN 6 (see subsection 'Cardiovascular disease') 867 patients were on premix insulin (with or without OAD(s)) at baseline. HbA_{1c} at baseline was 8.8%, 8.9% and 8.9% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively. At week 30, the change in HbA_{1c} was -1.3%, -1.8% and -0.4% for semaglutide 0.5 mg, semaglutide 1 mg, and placebo, respectively.

Cardiovascular disease

In a 104-week double-blind trial (SUSTAIN 6), 3,297 patients with type 2 diabetes mellitus at high cardiovascular risk were randomised to either semaglutide 0.5 mg once weekly, semaglutide 1 mg once weekly or corresponding placebo in addition to standard-of-care hereafter followed for 2 years. In total 98% of the patients completed the trial and the vital status was known at the end of the trial for 99.6% of the patients.

The trial population was distributed by age as: 1,598 patients (48.5%) ≥65 years, 321 (9.7%) ≥75 years, and 20 (0.6%) ≥85 years. There were 2,358 patients with normal or mild renal impairment, 832 with moderate and 107 with severe or end stage renal impairment. There were 61% males, the mean age was 65 years and mean BMI was 33 kg/m². The mean duration of diabetes was 13.9 years.

The primary endpoint was time from randomisation to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke.

The total number of primary component MACE endpoints was 254, including 108 (6.6%) with semaglutide and 146 (8.9%) with placebo. See figure 4 for results on primary and secondary cardiovascular endpoints. Treatment with semaglutide resulted in a 26% risk reduction in the primary composite outcome of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke. The total numbers of cardiovascular deaths, non-fatal

myocardial infarctions and non-fatal strokes were 90, 111, and 71, respectively, including 44 (2.7%), 47 (2.9%), and 27 (1.6%), respectively, with semaglutide (figure 4). The risk reduction in the primary composite outcome was mainly driven by decreases in the rate of non-fatal stroke (39%) and non-fatal myocardial infarction (26%) (figure 3).

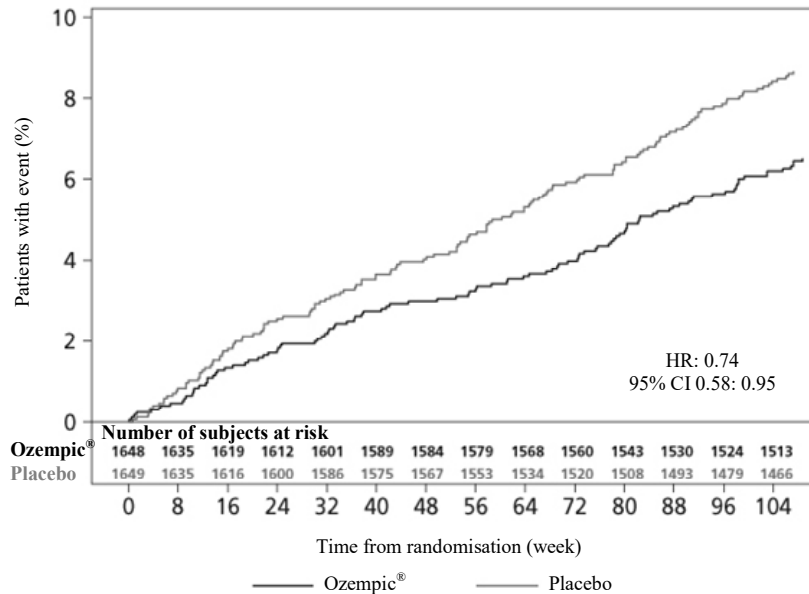


Figure 3 Kaplan-Meier plot of time to first occurrence of the composite outcome: cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (SUSTAIN 6)

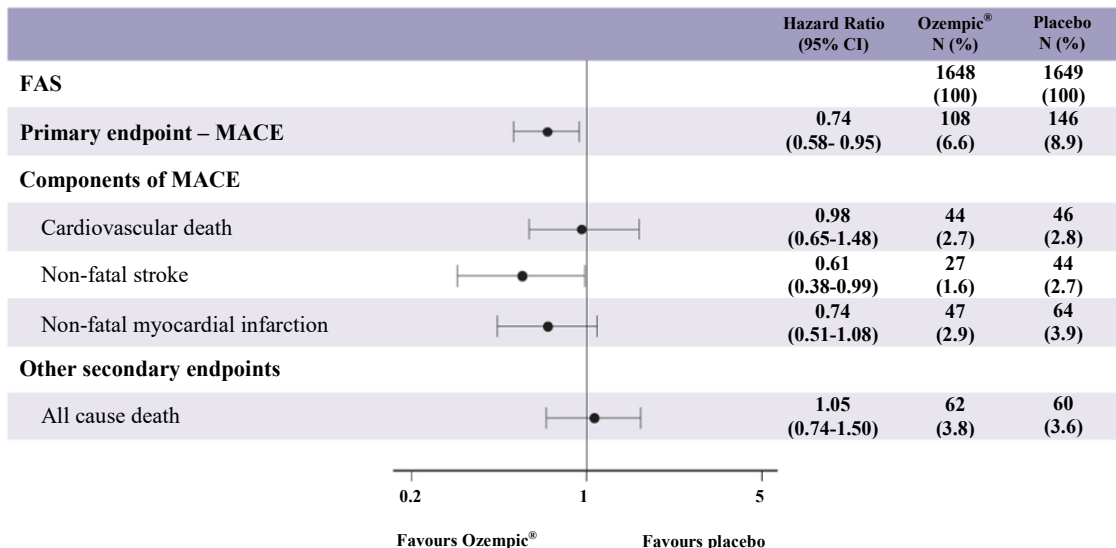


Figure 4 Forest plot: analyses of time to first occurrence of the composite outcome, its components and all cause death (SUSTAIN 6)

There were 158 events of new or worsening nephropathy. The hazard ratio [95% CI] for time to nephropathy (new onset of persistent macroalbuminuria, persistent doubling of serum

creatinine, need for continuous renal replacement therapy and death due to renal disease) was 0.64 [0.46; 0.88] driven by new onset of persistent macroalbuminuria.

Body weight

After one year of treatment, a weight loss of $\geq 5\%$ and $\geq 10\%$ was achieved for more subjects with semaglutide 0.5 mg (46% and 13%) and 1 mg (52–62% and 21–24%) compared with the active comparators sitagliptin (18% and 3%) and exenatide ER (17% and 4%).

In the 40-week trial vs. dulaglutide a weight loss of $\geq 5\%$ and $\geq 10\%$ was achieved for more subjects with semaglutide 0.5 mg (44% and 14%) compared with dulaglutide 0.75 mg (23% and 3%) and semaglutide 1 mg (up to 63% and 27%) compared with dulaglutide 1.5 mg (30% and 8%).

A significant and sustained reduction in body weight from baseline to week 104 was observed with semaglutide 0.5 mg and 1 mg vs. placebo 0.5 mg and 1 mg, in addition to standard-of-care (-3.6 kg and -4.9 kg vs. -0.7 kg and -0.5 kg, respectively) in SUSTAIN 6.

Blood pressure

Significant reductions in mean systolic blood pressure were observed when semaglutide 0.5 mg (3.5–5.1 mmHg) and 1 mg (5.4–7.3 mmHg) were used in combination with oral antidiabetic medicinal products or basal insulin. For diastolic blood pressure, there were no significant differences between semaglutide and comparators.

5.2 Pharmacokinetic properties

Compared to native GLP-1, semaglutide has a prolonged half-life of around 1 week making it suitable for once weekly subcutaneous 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.

Absorption

Maximum concentration was reached 1 to 3 days post dose. Steady state exposure was achieved following 4–5 weeks of once weekly administration. In patients with type 2 diabetes, the mean steady state concentrations following subcutaneous administration of 0.5 mg and 1 mg semaglutide were approximately 16 nmol/l and 30 nmol/l, respectively. Semaglutide exposure increased in a dose proportional manner for doses of 0.5 mg and 1 mg. Similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm. Absolute bioavailability of subcutaneous semaglutide was 89%.

Distribution

The mean volume of distribution of semaglutide following subcutaneous administration in patients with type 2 diabetes was approximately 12.5 l. Semaglutide was extensively bound to plasma albumin (>99%).

Biotransformation

Prior to excretion, semaglutide is extensively metabolised through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain. The enzyme neutral endopeptidase (NEP) is expected to be involved in the metabolism of semaglutide.

Elimination

In a trial with a single subcutaneous dose of radiolabelled semaglutide, it was found that the primary excretion routes of semaglutide-related material were via urine and faeces; approximately 2/3 of semaglutide-related material were excreted in urine and approximately 1/3 in faeces. Approximately 3% of the dose was excreted as intact semaglutide via urine. In patients with type 2 diabetes clearance of semaglutide was approximately 0.05 l/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 weeks after the last dose.

Special population

Elderly

Age had no effect on the pharmacokinetics of semaglutide based on data from phase 3a studies including patients of 20–86 years of age.

Gender, race and ethnicity

Gender, race (White, Black or African-American, Asian) and ethnicity (Hispanic or Latino, non-Hispanic or -Latino) had no effect on the pharmacokinetics of semaglutide.

Body weight

Body weight has an effect on the exposure of semaglutide. Higher body weight results in lower exposure; a 20% difference in body weight between individuals will result in an approximate 16% difference in exposure. Semaglutide doses of 0.5 mg and 1 mg provide adequate systemic exposure over a body weight range of 40–198 kg.

Renal impairment

Renal impairment did not impact the pharmacokinetics of semaglutide in a clinically relevant manner. This was shown with a single dose of 0.5 mg semaglutide for patients with different degrees of renal impairment (mild, moderate, severe or patients in dialysis) compared with subjects with normal renal function. This was also shown for subjects with type 2 diabetes and with renal impairment based on data from phase 3a studies, although the experience in patients with end-stage renal disease was limited.

Hepatic impairment

Hepatic impairment did not have any impact on the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated in patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function in a trial with a single-dose of 0.5 mg semaglutide.

Paediatric population

Semaglutide has not been studied in paediatric patients.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeat-dose toxicity or genotoxicity.

Non-lethal thyroid C-cell tumours observed in rodents are a class effect for GLP-1 receptor agonists. In 2-year carcinogenicity studies in rats and mice, semaglutide caused thyroid C-cell tumours at clinically relevant exposures. No other treatment-related tumours were observed. The rodent C-cell tumours are caused by a non-genotoxic, specific GLP-1 receptor mediated mechanism to which rodents are particularly sensitive. The relevance for humans is considered to be low, but cannot be completely excluded.

In fertility studies in rats, semaglutide did not affect mating performance or male fertility. In female rats, an increase in oestrous cycle length and a small reduction in *corpora lutea* (ovulations) were observed at doses associated with maternal body weight loss.

In embryo-foetal development studies in rats, semaglutide caused embryotoxicity below clinically relevant exposures. Semaglutide caused marked reductions in maternal body weight and reductions in embryonic survival and growth. In foetuses, major skeletal and visceral malformations were observed, including effects on long bones, ribs, vertebrae, tail, blood vessels and brain ventricles. Mechanistic evaluations indicated that the embryotoxicity involved a GLP-1 receptor mediated impairment of the nutrient supply to the embryo across the rat yolk sac. Due to species differences in yolk sac anatomy and function, and due to lack of GLP-1 receptor expression in the yolk sac of non-human primates, this mechanism is considered unlikely to be of relevance to humans. However, a direct effect of semaglutide on the foetus cannot be excluded.

In developmental toxicity studies in rabbits and *cynomolgus* monkeys, increased pregnancy loss and slightly increased incidence of foetal abnormalities were observed at clinically relevant exposures. The findings coincided with marked maternal body weight loss of up to 16%. Whether these effects are related to the decreased maternal food consumption as a direct GLP-1 effect is unknown.

Postnatal growth and development were evaluated in *cynomolgus* monkeys. Infants were slightly smaller at delivery, but recovered during the lactation period.

In juvenile rats, semaglutide caused delayed sexual maturation in both males and females. These delays had no impact upon fertility and reproductive capacity of either sex, or on the ability of the females to maintain pregnancy.

6.1 List of excipients

Disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and water for injections.

6.2 Incompatibilities

In the absence of compatibility studies this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

36 months

Before first use

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Expiry date is stated on the blister package and carton after 'Expiry'.

After first opening

In-use shelf life: 6 weeks

Store below 30 °C or in a refrigerator (2 °C – 8 °C). Do not freeze Ozempic®. Keep the pen cap on when the pen is not in use in order to protect it from light.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Keep away from the cooling element.
Do not freeze Ozempic®.

Keep the pen cap on in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

3 ml glass cartridge (type I glass) closed at the one end with a rubber plunger (chlorobutyl) and at the other end with an aluminium cap with a laminated rubber sheet (bromobutyl/polyisoprene) inserted. The cartridge is assembled into a disposable pre-filled pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

Pack size

1 pre-filled pen and 4 disposable NovoFine® Plus needles.

Each pre-filled pen contains 3 ml of solution, delivering doses of 1 mg.

HARUS DENGAN RESEP DOKTER

Reg. No.: DKXXXXXXXXXXXX

6.6 Special precautions for disposal and other handling

The patient should be advised to discard the injection needle after each injection and store the pen without an injection needle attached. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.

The pen is for use by one person only.

Ozempic® should not be used if it does not appear clear and colourless or almost colourless.

Ozempic® should not be used if it has been frozen.

Ozempic® can be administered with 30G, 31G, and 32G disposable needles up to a length of 8 mm.

Any unused medicinal product and other waste material should be disposed of in accordance with local requirements.

7. Manufactured by:

Novo Nordisk A/S

Brennum Park

DK-3400 Hillerød

STF NOV 2022

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Denmark

Released by:

Novo Nordisk A/S

Novo Allé

DK-2880 Bagsværd

Denmark

Registered by:

PT Beta Pharmacon

Indonesia

Distributed by:

PT Anugrah Argon Medica

Indonesia

Based on approval date:

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Novo Nordisk A/S

Ozempic®

1.34 mg/ml

1 mg/dose

solution for injection in pre-filled pen

semaglutide

Instructions on how to use Ozempic® 1 mg solution for injection in pre-filled pen

Please read these instructions carefully before using your Ozempic® pre-filled pen.

Talk to your doctor, nurse or pharmacist about how to inject Ozempic® correctly.

Start by checking your pen to **make sure that it contains Ozempic® 1 mg**, then look at the illustrations below to get to know the different parts of your pen and needle.

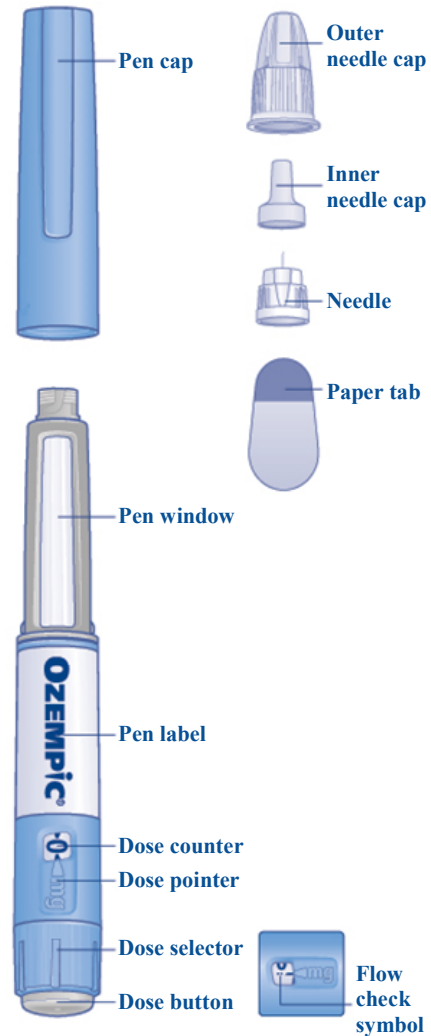
If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who knows how to use the Ozempic® pre-filled pen.

Your pen is a pre-filled dial-a-dose pen. It contains 4 mg of semaglutide, and you can only select doses of 1 mg. One unused pen contains four doses of 1 mg.

Use the table inside the lid of the carton to keep track of how many injections you have taken and when you took the injections.

Your pen is designed to be used with 30G, 31G, and 32G disposable needles up to a length of 8 mm. NovoFine® Plus needles are included in the pack.

Ozempic® pre-filled pen and needle (example)

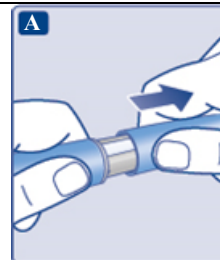


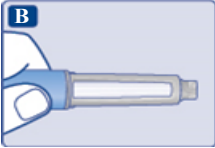
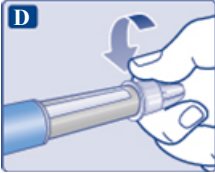
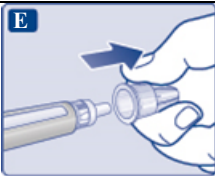
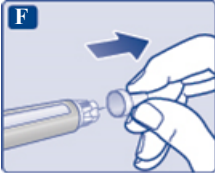
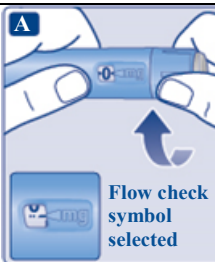
Important information

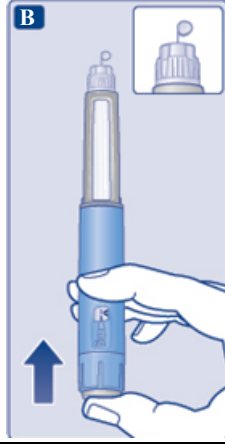
Pay special attention to these notes, as they are important for safe use of the pen.

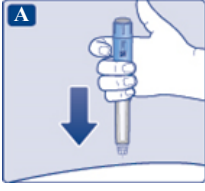
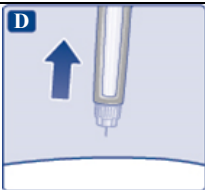
1. Prepare your pen with a new needle

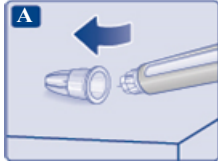
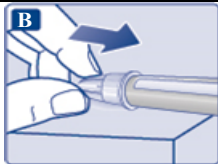
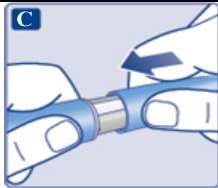
- **Check the name and coloured label** of your pen, to make sure that it contains Ozempic® 1 mg. This is especially important if you take more than one type of injectable medicine. Using the wrong medicine could be harmful to your health.
- **Pull off the pen cap.**



• Check that the solution in your pen is clear and colourless. Look through the pen window. If the solution looks cloudy or coloured, do not use the pen.	
• Take a new needle. Check the paper tab and the outer needle cap for damages that could affect sterility. If any damage is seen use a new needle. • Tear off the paper tab.	
Make sure to attach the needle correctly. • Push the needle straight onto the pen. • Turn until it is on tight.	
The needle is covered by two caps. You must remove both caps. If you forget to remove both caps, you will not inject any solution. • Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen.	
• Pull off the inner needle cap and throw it away. If you try to put it back on, you may accidentally stick yourself with the needle. A drop of solution may appear at the needle tip. This is normal, but you must still check the flow, if you use a new pen for the first time. See step 2 'Check the flow with each new pen'. Do not attach a new needle to your pen until you are ready to take your injection.	
 Always use a new needle for each injection. This may prevent blocked needles, contamination, infection and inaccurate dosing	
 Never use a bent or damaged needle.	
2. Check the flow with each new pen	
• If your pen is already in use, go to step 3 'Select your dose'. Only check the flow before your first injection with each new pen. • Turn the dose selector to the flow check symbol (•• —) right past '0'. Make sure the flow check symbol lines up with the pointer.	

Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter returns to '0'. The '0' must line up with the dose pointer. A drop of solution should appear at the needle tip.	
A small drop may remain at the needle tip, but it will not be injected. If no drop appears, repeat step 2 'Check the flow with each new pen' up to 6 times. If there is still no drop, change the needle and repeat step 2 'Check the flow with each new pen' once more. Dispose of the pen and use a new one if a drop of solution still does not appear.	
⚠ Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that the solution flows. If no drop appears, you will not inject any medicine even though the dose counter may move. This may indicate a blocked or damaged needle. If you do not check the flow before your first injection with each new pen, you may not get the prescribed dose and the intended effect of Ozempic®.	
3. Select your dose	
Turn the dose selector to select 1 mg. Keep turning until the dose counter stops and shows 1 mg.	
Only the dose counter and dose pointer will show that 1 mg has been selected. You can only select 1 mg per dose. When your pen contains less than 1 mg, the dose counter stops before 1 is shown. The dose selector clicks differently when turned forwards, backwards or past 1 mg. Do not count the pen clicks.	
⚠ Always use the dose counter and the dose pointer to see that 1 mg has been selected before injecting this medicine. Do not count the pen clicks. 1 mg must line up precisely with the dose pointer to ensure that you get a correct dose.	
How much solution is left	

• To see how much solution is left, use the dose counter: Turn the dose selector until the dose counter stops. If it shows 1, at least 1 mg is left in your pen. If the dose counter stops before 1 mg, there is not enough solution left for a full dose of 1 mg.	 Dose counter stopped: 1 mg left
⚠ If there is not enough solution left in your pen for a full dose, do not use it. Use a new Ozempic® pen.	
4. Inject your dose	
• Insert the needle into your skin as your doctor or nurse has shown you. • Make sure you can see the dose counter. Do not cover it with your fingers. This could interrupt the injection.	
• Press and hold down the dose button. Watch as the dose counter returns to '0'. The '0' must line up with the dose pointer. You may then hear or feel a click. • Continue pressing the dose button while keeping the needle in your skin.	
• Count slowly to 6, while keeping the dose button pressed. • If the needle is removed earlier, you may see a stream of solution coming from the needle tip. If so, the full dose will not be delivered.	 Count slowly: 1-2-3-4-5-6
• Remove the needle from your skin. You can then release the dose button. If blood appears at the injection site, press lightly.	
You may see a drop of solution at the needle tip after injecting. This is normal and does not affect your dose.	
⚠ Always watch the dose counter to know how many mg you inject. Hold the dose button down until the dose counter returns to '0'. How to identify a blocked or damaged needle – If '0' does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle. – In this case, you have not received any medicine – even though the dose counter has moved from the original dose that you have set. How to handle a blocked needle	

Change the needle as described in step 5 'After your injection' and repeat all steps starting with step 1 'Prepare your pen with a new needle'. Make sure you select the full dose you need. Never touch the dose counter when you inject. This can interrupt the injection.	
5. After your injection	
Always dispose of the needle after each injection to ensure convenient injections and prevent blocked needles. If the needle is blocked, you will not inject any medicine. • Lead the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap.	
• Once the needle is covered, carefully push the outer needle cap completely on. • Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities.	
• Put the pen cap on your pen after each use to protect the solution from light.	
When the pen is empty, throw it away without a needle on as instructed by your doctor, nurse, pharmacist or local authorities.	
⚠ Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.	
⚠ Always remove the needle from your pen immediately after each injection. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.	
⚠ Further important information	
• Always keep your pen and needles out of the sight and reach of others, especially children. • Never share your pen or your needles with other people. • Caregivers must be very careful when handling used needles to prevent needle injury and cross-infection.	
Caring for your pen	
Treat your pen with care. Rough handling or misuse may cause inaccurate dosing. If this happens you might not get the intended effect of this medicine.	
• Do not leave the pen in a car or another place where it can get too hot or too cold. • Do not inject Ozempic® which has been frozen. If you do that, you might not get the intended effect of this medicine. • Do not inject Ozempic® which has been exposed to direct sunlight. If you do that, you might not get the intended effect of this medicine. • Do not expose your pen to dust, dirt or liquid. • Do not wash, soak or lubricate your pen. It may be cleaned with a mild detergent on a	

moistened cloth.

- **Do not drop your pen** or knock it against hard surfaces. If you drop it or suspect a problem, attach a new needle and check the flow before you inject.
- **Do not try to refill your pen.** Once empty, it must be disposed of.
- **Do not try to repair your pen** or pull it apart.

Brosur kemasan: Informasi untuk pasien

Ozempic®

1,34 mg/ml

1 mg/dosis

**Larutan injeksi dalam pena yang sudah terisi
semaglutide**

Bacalah seluruh brosur ini dengan teliti sebelum Anda mulai menggunakan obat ini karena brosur ini berisi informasi yang penting untuk Anda.

- Simpan brosur ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini mungkin membahayakan mereka, meskipun jika mereka memiliki tanda – tanda sakit yang sama dengan Anda.
- Jika Anda mengalami efek samping apapun, bicarakan dengan dokter, apoteker atau perawat Anda. Termasuk kemungkinan efek samping apapun yang tidak tercantum dalam brosur ini. Lihat bagian 4 *Efek samping yang mungkin dirasakan*.

Apa yang terdapat dalam brosur ini

1. Apa itu Ozempic® dan untuk apa kegunaannya
2. Apa yang Anda perlu ketahui sebelum menggunakan Ozempic®
3. Bagaimana cara menggunakan Ozempic®
4. Efek samping yang mungkin dirasakan
5. Bagaimana cara menyimpan Ozempic®
6. Isi kemasan dan informasi lain

1. Apa itu Ozempic® dan untuk apa kegunaannya

Ozempic® berisi zat aktif semaglutide. Zat aktif tersebut membantu tubuh Anda mengurangi kadar gula darah Anda hanya ketika kadar gula darah terlalu tinggi dan dapat membantu mencegah penyakit jantung.

Ozempic® digunakan untuk pengobatan orang dewasa (usia 18 tahun dan ke atas) dengan diabetes mellitus tipe 2 ketika diet dan olahraga bersama dengan obat – obat diabetes lain tidak cukup untuk mengontrol kadar gula darah Anda. Obat – obatan lain ini mungkin digunakan secara oral atau suntikan meliputi metformin, metformin dan sulfonilurea, metformin dan insulin basal, atau *sodium-glucose cotransporter 2 (SGLT2) inhibitor*.

Penting bahwa Anda terus melanjutkan rencana diet dan olahraga Anda sebagaimana yang diberitahu oleh dokter, apoteker atau perawat Anda.

2. Apa yang Anda perlu ketahui sebelum menggunakan Ozempic®

Jangan menggunakan Ozempic®

- jika Anda alergi terhadap semaglutide atau salah satu zat lain dari obat ini (yang tercantum dalam bagian 6 *Isi kemasan dan informasi lain*).

Peringatan dan pencegahan

Bicarakan dengan dokter, apoteker atau perawat Anda sebelum menggunakan obat ini.

Obat ini tidak sama dengan insulin dan Anda seharusnya tidak menggunakannya jika:

- Anda memiliki diabetes tipe 1 – suatu kondisi dimana tubuh Anda tidak memproduksi insulin apapun
- Anda memiliki penyakit yang mengarah ke diabetes ketoasidosis – komplikasi diabetes dengan kadar gula darah yang tinggi, kesulitan bernapas, kebingungan, rasa haus yang berlebihan, bau manis di nafas atau rasa manis atau logam di mulut.

Ozempic® bukan insulin dan seharusnya tidak digunakan sebagai pengganti insulin.

Efek terhadap sistem pencernaan

Selama pengobatan dengan obat ini, Anda mungkin merasa mual atau muntah, atau diare. Efek samping tersebut dapat menyebabkan dehidrasi (kehilangan cairan). Penting untuk Anda minum cairan yang banyak untuk mencegah dehidrasi. Hal tersebut penting terutama jika Anda memiliki gangguan ginjal. Bicarakan dengan dokter Anda jika Anda memiliki pertanyaan atau pertimbangan.

Nyeri perut yang parah dan berkelanjutan yang dapat disebabkan oleh pankreatitis akut

Jika Anda mengalami nyeri yang parah dan berkelanjutan di daerah perut - langsung temui dokter karena hal tersebut dapat menjadi tanda pankreatitis akut (radang pankreas). Lihat bagian 4 *Efek samping yang mungkin dirasakan* untuk tanda – tanda peringatan radang pankreas.

Kadar gula darah yang rendah (hipoglikemia)

Mengkombinasikan sulfonilurea atau insulin dengan obat ini mungkin meningkatkan risiko terkena kadar gula darah yang rendah (hipoglikemia). Lihat bagian 4 untuk tanda – tanda peringatan dari kadar gula darah yang rendah. Dokter Anda mungkin meminta Anda untuk memeriksa kadar gula darah Anda. Hal tersebut akan membantu dokter memutuskan apakah dosis sulfonilurea atau insulin perlu diubah untuk mengurangi risiko kadar gula darah yang rendah.

Penyakit mata diabetes (retinopati)

Jika Anda memiliki penyakit mata diabetes dan sedang menggunakan insulin, obat ini mungkin menyebabkan memburuknya penglihatan Anda, dan mungkin memerlukan pengobatan. Beritahu dokter Anda jika Anda memiliki penyakit mata diabetes atau jika Anda mengalami gangguan mata selama pengobatan dengan obat ini.

Anak-anak dan remaja

Obat ini tidak direkomendasikan untuk anak-anak dan remaja usia di bawah 18 tahun karena keamanan dan khasiat dalam kelompok usia tersebut belum dikembangkan.

Obat – obatan lain dan Ozempic®

Beritahu dokter, apoteker atau perawat Anda jika Anda sedang mengonsumsi, baru-baru ini sudah mengonsumsi, atau mungkin mengonsumsi obat lain, termasuk obat – obatan herbal atau obat lain yang Anda beli tanpa resep.

Tidak ada penyesuaian dosis parasetamol, kontrasepsi oral, atorvastatin, digoksin dan metformin ketika digunakan bersama dengan semaglutide.

Secara khusus, beritahu dokter, apoteker atau perawat Anda jika Anda menggunakan obat – obatan yang mengandung salah satu zat berikut:

- Warfarin atau obat serupa lainnya yang dikonsumsi secara oral untuk mengurangi pembekuan darah (anti koagulan oral). Anda mungkin memerlukan pemeriksaan darah yang sering untuk memeriksa seberapa cepat darah Anda membeku.
- Jika Anda sedang menggunakan insulin, dokter Anda akan memberitahu Anda bagaimana cara mengurangi dosis insulin dan akan merekomendasikan Anda untuk lebih sering memantau kadar gula darah Anda untuk menghindari hiperglikemia (kadar gula darah yang tinggi) dan diabetes ketoasidosis (komplikasi diabetes yang terjadi ketika tubuh tidak dapat memecah glukosa karena tidak terdapat cukup insulin).

Kehamilan dan menyusui

Jika Anda sedang hamil atau menyusui, merasa Anda mungkin hamil, atau berencana untuk punya anak, mintalah saran kepada dokter Anda sebelum menggunakan obat ini.

Obat ini seharusnya tidak digunakan selama kehamilan, karena belum diketahui apakah obat ini memengaruhi janin. Oleh karena itu, penggunaan kontrasepsi direkomendasikan ketika menggunakan obat ini. Jika Anda ingin hamil, diskusikan bagaimana mengubah pengobatan Anda dengan dokter Anda karena Anda seharusnya berhenti menggunakan obat ini setidaknya 2 bulan sebelumnya. Jika Anda hamil ketika menggunakan obat ini, bicarakan dengan dokter Anda segera, karena pengobatan Anda akan perlu diubah.

Jangan menggunakan obat ini jika Anda sedang menyusui, karena belum diketahui apakah obat ini masuk ke dalam ASI.

Mengemudi dan menjalankan mesin

Ozempic® hampir tidak memengaruhi kemampuan Anda mengemudi atau menggunakan mesin. Jika Anda menggunakan obat ini dikombinasikan dengan sulfonilurea atau insulin, kadar gula darah yang rendah (hipoglikemia) dapat terjadi yang mungkin mengurangi kemampuan Anda untuk berkonsentrasi. Jangan mengemudi atau menjalankan mesin jika Anda mengalami tanda – tanda kadar gula darah yang rendah. Lihat bagian 2, *Peringatan dan pencegahan* untuk informasi tentang peningkatan risiko kadar gula darah yang rendah dan bagian 4 untuk tanda – tanda peringatan kadar gula darah yang rendah. Bicarakan dengan dokter Anda untuk informasi lebih lanjut.

Kandungan natrium

Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per dosis, pada dasarnya 'bebas natrium'.

3. Bagaimana cara menggunakan Ozempic®

Selalu gunakan obat ini sama seperti yang diberitahu oleh dokter Anda. Periksa dengan dokter, apoteker atau perawat Anda jika Anda tidak yakin.

Berapa banyak yang digunakan

- Dosis awal adalah 0,25 mg seminggu sekali selama empat minggu.
- Setelah empat minggu dokter Anda akan meningkatkan dosis menjadi 0,5 mg seminggu sekali.
- Dokter mungkin meningkatkan dosis Anda ke 1 mg seminggu sekali jika kadar gula darah Anda tidak terkontrol dengan cukup baik dengan dosis 0,5 mg seminggu sekali.

Jangan mengubah dosis Anda kecuali diberitahu oleh dokter Anda.

Bagaimana Ozempic® diberikan

Ozempic® diberikan sebagai suntikan di bawah kulit (injeksi subkutan). Jangan menyuntikkan ke dalam pembuluh darah atau otot.

- Tempat terbaik untuk penyuntikan adalah paha depan, bagian depan pinggang (perut), atau lengan atas Anda.
- Sebelum menggunakan pena untuk pertama kalinya, dokter atau perawat Anda akan menunjukkan kepada Anda bagaimana cara menggunakannya.

Instruksi penggunaan yang detail ada di sisi lain dari brosur kemasan ini.

Kapan menggunakan Ozempic®

- Anda seharusnya menggunakan obat ini seminggu sekali di hari yang sama setiap minggu jika memungkinkan.
- Anda dapat melakukan penyuntikan kapanpun sepanjang hari – tidak tergantung makanan.

Untuk membantu mengingatkan Anda melakukan penyuntikan obat ini seminggu sekali saja, direkomendasikan untuk mencatat hari kerja sebagai pilihan (misalnya Rabu) di karton dan menulis tanggal di karton setiap kali Anda sudah menyuntikkannya.

Jika perlu Anda dapat mengubah hari penyuntikan mingguan Anda dari obat ini selama sudah berjalan setidaknya 3 hari sejak penyuntikan terakhir Anda. Setelah memilih hari yang baru, lanjutkan dengan dosis seminggu sekali.

Jika Anda menggunakan Ozempic® lebih banyak dari yang seharusnya

Jika Anda menggunakan Ozempic® lebih banyak dari yang seharusnya, langsung bicarakan dengan dokter Anda. Anda mungkin mengalami efek samping seperti perasaan mual.

Jika Anda lupa untuk menggunakan Ozempic®

Jika Anda lupa menyuntikkan satu dosis dan:

- sudah 5 hari atau kurang dari yang Anda seharusnya menggunakan Ozempic®, gunakan sesegera mungkin setelah Anda ingat. Kemudian suntikkan dosis berikutnya seperti biasa di hari yang sudah Anda jadwalkan.

- sudah lebih dari 5 hari sejak Anda seharusnya menggunakan Ozempic®, lewati dosis yang terlupa. Kemudian suntikkan dosis berikutnya seperti biasa di hari yang sudah Anda jadwalkan.

Jangan menggunakan dosis ganda untuk mengganti dosis yang terlupa.

Jika Anda berhenti menggunakan Ozempic®

Jangan berhenti menggunakan obat ini tanpa berbicara dengan dokter Anda. Jika Anda berhenti menggunakannya, kadar gula darah Anda mungkin naik.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter, apoteker atau perawat Anda.

4. Efek samping yang mungkin dirasakan

Seperti semua obat – obatan, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping yang serius

Umum (mungkin memengaruhi hingga 1 dari 10 orang)

- komplikasi dari penyakit mata diabetes (retinopati) - Anda seharusnya memberitahu dokter Anda jika Anda mengalami gangguan mata, seperti perubahan di pandangan, selama pengobatan dengan obat ini.

Tidak umum (mungkin memengaruhi hingga 1 dari 100 orang)

- inflamasi pankreas (pankreatitis akut) yang dapat menyebabkan nyeri parah di lambung dan punggung yang tidak hilang. Anda seharusnya segera ke dokter jika Anda mengalami gejala tersebut.

Jarang (mungkin memengaruhi hingga 1 dari 1.000 orang)

- reaksi alergi yang parah (reaksi anafilaksis, angioedema). Anda harus segera mendapatkan bantuan medis dan langsung menginformasikan dokter Anda jika Anda mendapatkan gejala seperti gangguan pernapasan, pembengkakan di wajah, bibir, lidah dan/atau tenggorokan dengan kesulitan menelan dan detak jantung yang cepat.

Efek samping lain

Sangat umum (mungkin memengaruhi lebih dari 1 dari 10 orang)

- mual – biasanya hilang seiring waktu
- diare – biasanya hilang seiring waktu.
- kadar gula yang rendah (hipoglikemia) ketika obat ini digunakan dengan obat yang mengandung sulfonilurea atau insulin

Umum (mungkin memengaruhi hingga 1 dari 10 orang)

- muntah
- kadar gula darah yang rendah (hipoglikemia) ketika obat ini digunakan dengan obat antidiabetes oral selain sulfonilurea atau insulin.

Tanda – tanda peringatan kadar gula darah yang rendah mungkin datang tiba-tiba. Tanda – tanda tersebut dapat mencakup: keringat dingin, kulit pucat dingin, sakit kepala, detak jantung cepat, mual atau sangat lapar, perubahan pandangan, merasa mengantuk atau lemah, merasa gugup, cemas atau bingung, kesulitan berkonsentrasi atau gemetar. Dokter Anda akan memberitahu Anda bagaimana cara mengobati kadar gula darah yang rendah dan apa yang dilakukan jika Anda melihat tanda – tanda peringatan tersebut. Kadar gula darah yang rendah lebih mungkin terjadi jika Anda juga mengonsumsi sulfonilurea atau insulin. Dokter Anda mungkin mengurangi dosis obat – obatan tersebut sebelum Anda mulai menggunakan obat ini.

- gangguan pencernaan
- radang perut (gastritis) – tanda – tanda termasuk sakit perut, mual atau muntah
- refluks atau rasa panas di perut - juga disebut *gastro-esophageal reflux disease* (GERD)
- nyeri perut
- perut kembung
- konstipasi
- sendawa
- batu empedu
- pusing
- kelelahan
- penurunan berat badan
- kurang nafsu makan
- kentut (flatulensi)
- peningkatan enzim pankreas (seperti lipase dan amilase).

Tidak umum (mungkin memengaruhi hingga 1 dari 100 orang)

- perubahan rasa makanan atau minuman
- denyut nadi cepat
- reaksi di tempat penyuntikan - seperti memar, nyeri, iritasi, gatal dan ruam
- reaksi alergi seperti ruam, gatal atau bentol
- penundaan pengosongan lambung.

Pelaporan efek samping

Jika Anda mengalami efek samping apapun, bicarakan dengan dokter, apoteker atau perawat Anda. Hal tersebut termasuk efek samping yang mungkin tidak tercantum dalam brosur ini. Dengan melaporkan efek samping Anda dapat membantu menyediakan lebih banyak informasi keamanan obat ini.

5. Bagaimana cara menyimpan Ozempic®

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan obat ini setelah tanggal kadaluwarsa yang tertera di label pena dan karton setelah 'Expiry'. Tanggal kadaluwarsa mengacu di hari terakhir dari bulan tersebut.

Sebelum dibuka:

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Simpan di lemari pendingin (2°C - 8°C). Jangan dibekukan. Jauhkan dari elemen pendingin. Pasang tutup pena untuk melindunginya dari cahaya.

Selama penggunaan:

- Anda dapat menyimpan pena selama 6 minggu jika disimpan di suhu di bawah 30°C atau dalam lemari pendingin (2°C - 8°C) jauh dari elemen pendingin. Jangan membekukan Ozempic® dan jangan menggunakannya jika sudah membeku.
- Ketika Anda tidak menggunakan pena, pasang tutup pena untuk melindunginya dari cahaya.

Jangan menggunakan obat ini jika Anda melihat bahwa larutan obat ini tidak jernih dan tidak berwarna atau hampir tidak berwarna.

Jangan membuang obat – obatan melalui air limbah atau sampah rumah tangga. Tanyakan kepada apoteker Anda bagaimana cara membuang obat – obatan yang Anda tidak lagi gunakan. Langkah-langkah tersebut akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lain

Apa kandungan Ozempic®

- Zat aktifnya adalah semaglutide. Larutan injeksi satu ml mengandung 1,34 mg semaglutide. Satu pena yang sudah terisi mengandung 2 mg semaglutide dalam 1,5 ml larutan.
- Zat lainnya adalah: dinatrium fosfat dihidrat, propilen glikol, fenol, air untuk injeksi, natrium hidroksida / asam hidroklorida (untuk penyesuaian pH). Lihat juga bagian 2 'Kandungan natrium'.

Seperti apa Ozempic® dan isiemasannya

Ozempic® adalah larutan injeksi jernih dan tidak berwarna atau hampir tidak berwarna dalam pena yang sudah terisi.

Setiap pena berisi 3 ml larutan, menyuntikkan dosis 1 mg.

Larutan injeksi Ozempic® 1 mg tersedia dalam kemasan berikut:

1 pena dan 4 jarum sekali pakai NovoFine® Plus.

HARUS DENGAN RESEP DOKTER

Reg. No.: DKIXXXXXXXXXXXXX

Diproduksi oleh:

Novo Nordisk A/S
Brennum Park
DK-3400 Hillerød
Denmark

Dirilis oleh:

Novo Nordisk A/S
Novo Alle

DK-2880 Bagsværd
Denmark

Didaftarkan oleh:

PT Beta Pharmacon
Indonesia

Didistribusikan oleh:

PT Anugrah Argon Medica
Indonesia

Berdasarkan persetujuan tanggal:

Ozempic® dan NovoFine® adalah merek dagang yang dimiliki oleh Novo Nordisk A/S, Denmark.

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Novo Nordisk A/S

Ozempic®

1,34 mg/ml

1 mg/dosis

larutan injeksi dalam pena yang sudah terisi

semaglutide

Instruksi bagaimana cara menggunakan Ozempic® 1 mg larutan injeksi dalam pena yang sudah terisi

Bacalah instruksi ini dengan teliti sebelum menggunakan pena yang sudah terisi Ozempic® Anda.

Bicarakan dengan dokter, perawat atau apoteker Anda tentang bagaimana menyuntikkan Ozempic® dengan benar.

Mulai dengan memeriksa pena Anda **untuk memastikan pena berisi Ozempic® 1 mg**, kemudian lihat gambar di bawah ini untuk mengenal bagian-bagian yang berbeda dari pena dan jarum Anda.

Jika Anda buta atau memiliki penglihatan yang buruk dan tidak dapat membaca penghitung dosis di pena, jangan menggunakan pena ini tanpa bantuan. Dapatkan bantuan dari seseorang dengan penglihatan yang baik yang mengetahui bagaimana menggunakan pena yang sudah terisi Ozempic®.

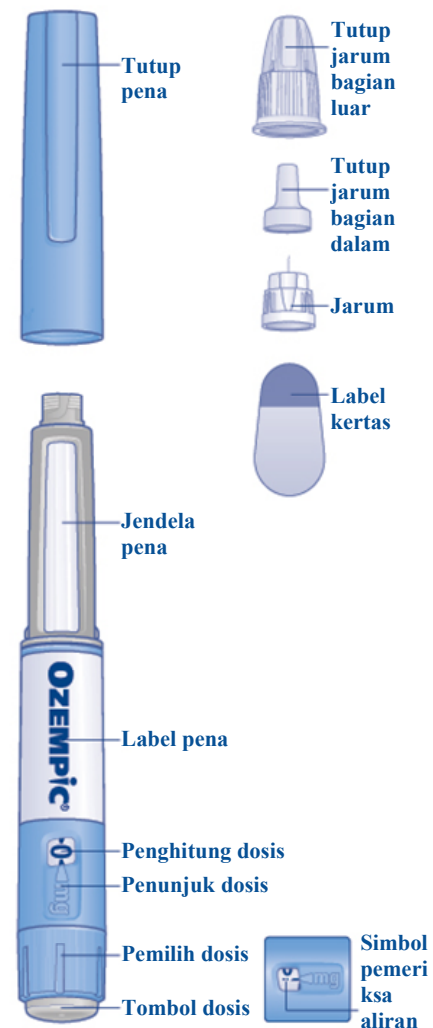
Pena Anda adalah pena *dial-a-dose* yang sudah terisi. Pena mengandung 4 mg semaglutide, dan Anda hanya dapat memilih dosis 1 mg. Satu pena yang belum digunakan mengandung empat dosis 1 mg.

Gunakan tabel di dalam karton untuk melacak berapa banyak penyuntikan yang telah Anda lakukan dan kapan Anda melakukan penyuntikan.

Pena Anda didesain untuk digunakan dengan jarum sekali pakai 30G, 31G dan 32G dengan panjang hingga 8 mm.

Jarum NovoFine® Plus sudah termasuk dalam kemasan.

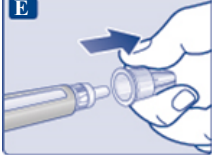
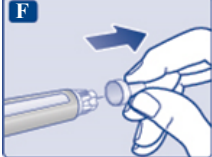
Pena yang sudah terisi Ozempic® dan jarum (contoh)



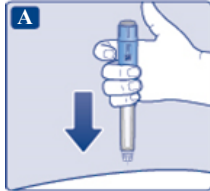
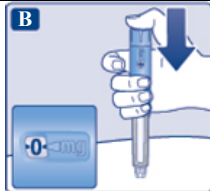
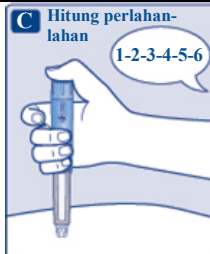
Informasi penting

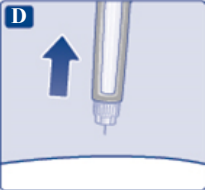
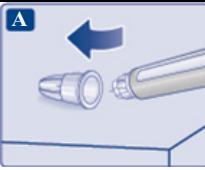
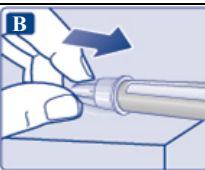
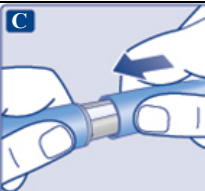
Berikan perhatian khusus di catatan ini, karena penting untuk penggunaan pena yang aman.

1. Mempersiapkan pena Anda dengan jarum baru

• Periksa nama dan label warna pena Anda, untuk memastikan bahwa pena berisi Ozempic® 1 mg. Hal tersebut terutama penting jika Anda mengonsumsi lebih dari satu jenis obat suntik. Menggunakan obat yang salah dapat berbahaya bagi kesehatan Anda. • Cabut tutup pena.		
• Periksa bahwa larutan dalam pena Anda jernih dan tidak berwarna. Lihat melalui jendela pena. Jika larutan terlihat keruh atau berwarna, jangan menggunakan pena.		
• Ambil jarum baru Periksa label kertas dan tutup jarum bagian luar untuk kerusakan yang dapat memengaruhi sterilitas. Jika terlihat kerusakan apapun gunakan jarum baru. • Lepaskan label kertasnya.		
Pastikan untuk memasang jarum dengan benar. • Tekan jarum lurus ke pena. • Putar hingga terpasang erat.		
Jarum tertutup oleh 2 tutup. Anda harus melepaskan kedua tutup. Jika Anda lupa melepaskan kedua tutup, Anda tidak akan menyuntikkan larutan apapun. • Cabut tutup jarum bagian luar dan simpan untuk nanti. Anda akan memerlukannya setelah penyuntikan, untuk melepaskan jarum dari pena dengan aman.		
• Cabut tutup jarum bagian dalam dan buang. Jika Anda mencoba untuk memasangnya kembali, Anda mungkin tertusuk jarum secara tidak sengaja. Setetes larutan mungkin muncul di ujung jarum. Hal tersebut normal, tetapi Anda tetap harus memeriksa aliran, jika Anda menggunakan pena baru untuk pertama kalinya. Lihat langkah 2 'Memeriksa aliran dengan setiap pena baru'. Jangan memasang jarum baru untuk pena Anda hingga Anda siap untuk melakukan penyuntikan Anda.		
 Selalu gunakan jarum baru untuk setiap penyuntikan. Hal tersebut mungkin mencegah jarum tersumbat, kontaminasi, infeksi dan dosis yang tidak akurat.		

⚠ Jangan pernah menggunakan jarum yang bengkok atau rusak.	
2. Memeriksa aliran dengan setiap pena baru	
- Jika pena Anda telah digunakan, lanjutkan ke langkah 3 'Memilih dosis Anda'. Periksa aliran hanya sebelum penyuntikan pertama Anda dengan setiap pena baru. - Putar pemilih dosis ke simbol pemeriksa aliran (•• —) tepat setelah '0'. Pastikan simbol pemeriksa aliran sejajar dengan penunjuk.	 Simbol pemeriksa aliran dipilih
Pegang pena dengan jarum mengarah ke atas. Tekan dan tahan tombol dosis hingga penghitung dosis kembali ke '0'. '0' harus sejajar dengan penunjuk dosis. Setetes larutan seharusnya muncul di ujung jarum.	
Sedikit tetesan mungkin tetap ada di ujung jarum, tetapi tidak akan disuntikkan. Jika tetesan tidak muncul, ulangi langkah 2 'Memeriksa aliran dengan setiap pena baru' hingga 6 kali. Jika masih tidak ada tetesan, ganti jarum dan ulangi langkah 2 'Memeriksa aliran dengan setiap pena baru' sekali lagi. Buang pena dan gunakan pena baru jika tetesan larutan masih tidak muncul.	
⚠ Selalu pastikan bahwa tetesan muncul di ujung jarum sebelum Anda menggunakan pena baru untuk pertama kalinya. Hal tersebut memastikan bahwa larutan mengalir. Jika tetesan tidak muncul, Anda tidak akan menyuntikkan obat apapun meskipun penghitung dosis mungkin bergerak. Hal tersebut mungkin menunjukkan jarum tersumbat atau rusak. Jika Anda tidak memeriksa aliran sebelum penyuntikan pertama Anda dengan masing-masing pena baru, Anda mungkin tidak mendapatkan dosis yang diresepkan dan efek yang diinginkan dari Ozempic®.	
3. Memilih dosis Anda	
Putar pemilih dosis untuk memilih 1 mg. Terus putar hingga penghitung dosis berhenti dan menunjukkan 1 mg.	 1 mg dipilih
Hanya penghitung dosis dan penunjuk dosis yang akan menunjukkan bahwa 1 mg sudah dipilih. Anda hanya dapat memilih 1 mg per dosis. Ketika pena Anda mengandung kurang dari 1 mg, penghitung dosis berhenti sebelum 1 ditunjukkan.	

Pilih dosis berbunyi klik berbeda ketika diputar ke depan, belakang atau melewati 1 mg. Jangan menghitung klik pena.	
⚠ Selalu gunakan penghitung dosis dan penunjuk dosis untuk melihat bahwa 1 mg sudah dipilih sebelum menyuntikkan obat ini. Jangan menghitung klik pena. 1 mg harus tepat sejajar dengan penunjuk dosis untuk memastikan bahwa Anda mendapatkan dosis yang benar.	
Berapa jumlah larutan yang tersisa	
Untuk melihat berapa jumlah larutan yang tersisa, Gunakan penghitung dosis: Putar pemilih dosis hingga penghitung dosis berhenti. Jika penghitung dosis menunjukkan 1, setidaknya 1 mg yang tersisa dalam pena Anda. - Jika penghitung dosis berhenti sebelum 1 mg, tidak ada cukup larutan yang tersisa untuk dosis penuh 1 mg.	
⚠ Jika tidak ada cukup larutan yang tersisa dalam pena Anda untuk dosis penuh, jangan menggunakannya. Gunakan pena Ozempic® yang baru.	
4. Menyuntikkan dosis Anda	
Masukkan jarum ke dalam kulit Anda sebagaimana yang ditunjukkan oleh dokter atau perawat Anda. Pastikan Anda dapat melihat penghitung dosis. Jangan menutupinya dengan jari-jari Anda. Hal tersebut dapat mengganggu penyuntikan.	
Tekan dan tahan tombol dosis. Lihat ketika penghitung dosis kembali ke '0'. '0' harus sejajar dengan penunjuk dosis. Anda kemudian mungkin mendengar atau merasakan klik. Terus tekan tombol dosis ketika jarum di dalam kulit Anda.	
Hitung perlahan-lahan hingga 6, ketika tombol dosis ditekan. - Jika jarum dicabut lebih cepat, Anda mungkin melihat aliran larutan yang berasal dari ujung jarum. Jika demikian, dosis penuh tidak akan didapatkan.	

• Lepaskan jarum dari kulit Anda. Anda dapat melepaskan tombol dosis. Jika darah muncul di lokasi penyuntikan, tekan perlahan.	
Anda mungkin melihat tetesan larutan di ujung jarum setelah penyuntikan. Hal tersebut normal dan tidak memengaruhi dosis Anda.	
⚠ Selalu perhatikan penghitung dosis untuk mengetahui berapa jumlah mg yang Anda suntikkan. Tahan tombol dosis ke bawah hingga penghitung dosis kembali ke '0'. Bagaimana mengidentifikasi jarum yang tersumbat atau rusak – Jika '0' tidak muncul di penghitung dosis setelah Anda terus menerus menekan tombol dosis, maka Anda mungkin sudah menggunakan jarum yang tersumbat atau rusak. – Dalam hal tersebut, Anda belum menerima obat apapun - meskipun penghitung dosis sudah bergerak dari dosis awal yang sudah diatur. Bagaimana menangani jarum yang tersumbat Ganti jarum seperti yang dijelaskan di langkah 5 'Setelah penyuntikan Anda' dan ulangi semua langkah dimulai dengan langkah 1 'Memersiapkan pena Anda dengan jarum baru'. Pastikan Anda memilih dosis penuh yang Anda perlukan. Jangan pernah menyentuh penghitung dosis ketika Anda menyuntikkan. Hal tersebut dapat mengganggu penyuntikan.	
5. Setelah penyuntikan Anda	
Selalu buang jarum setelah setiap penyuntikan untuk memastikan penyuntikan yang nyaman dan mencegah jarum tersumbat. Jika jarum tersumbat, Anda tidak akan menyuntikkan obat apapun. • Arahkan ujung jarum ke tutup jarum bagian luar di permukaan yang datar tanpa menyentuh jarum atau tutup jarum bagian luar.	
• Setelah jarum tertutup, dorong pelan-pelan tutup jarum bagian luar sepenuhnya. • Lepaskan jarum dan buang dengan hati-hati seperti yang diinstruksikan oleh dokter, perawat, apoteker atau pihak berwenang setempat Anda.	
• Pasang tutup pena di pena Anda setelah setiap penggunaan untuk melindungi larutan dari cahaya.	
Ketika pena kosong, buang pena tanpa jarum seperti yang diinstruksikan oleh dokter,	

perawat, apoteker atau pihak berwenang setempat Anda.	
⚠	Jangan pernah mencoba untuk memasang kembali tutup jarum bagian dalam. Anda mungkin tertusuk jarum.
⚠	Selalu lepaskan jarum dari pena Anda segera setelah setiap penyuntikan. Hal tersebut mungkin mencegah jarum tersumbat, kontaminasi, infeksi, kebocoran larutan dan dosis yang tidak akurat.
⚠	Informasi penting lebih lanjut
	- Selalu simpan pena dan jarum dari pandangan dan jangkauan orang lain, terutama anak-anak. Jangan pernah berbagi pena atau jarum Anda dengan orang lain. - Perawat harus sangat berhati-hati ketika menangani jarum bekas untuk mencegah cedera tertusuk jarum dan infeksi silang.
Pemeliharaan pena Anda	
Perlakukan pena Anda dengan hati-hati. Penanganan yang kasar atau penyalahgunaan dapat menyebabkan dosis yang tidak akurat. Jika hal tersebut terjadi, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini.	
	Jangan meninggalkan pena di dalam mobil atau tempat lain dimana pena dapat menjadi terlalu panas atau terlalu dingin. Jangan menyuntikkan Ozempic® yang sudah membeku. Jika Anda melakukannya, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini. Jangan menyuntikkan Ozempic® yang sudah terpapar sinar matahari langsung. Jika Anda melakukannya, Anda mungkin tidak mendapatkan efek yang diinginkan dari obat ini. Jangan memaparkan pena Anda ke debu, kotoran atau larutan. Jangan mencuci, merendam atau melumasi pena Anda. Pena mungkin dibersihkan dengan deterjen ringan di kain yang lembab. Jangan menjatuhkan pena Anda atau membenturkan di permukaan yang keras. Jika Anda menjatuhkannya atau menduga ada masalah, pasang jarum baru dan periksa aliran sebelum Anda menyuntikkan. Jangan mencoba untuk mengisi ulang pena Anda. Setelah habis, pena harus dibuang. Jangan mencoba untuk memperbaiki pena Anda atau memisahkan bagian – bagiannya.

Regulatory Operations

Carton: 2010-22-530-12-303
LIFT - Current 1

Lacquerform 30793-1
Lacquer free area: ■

Braille No.: XXXX-XX-X
Placement: Front

Ozempic 1 mg

Colour:
PMS 280C +
PMS 3155C +
PMS Cool Gray 6C +
PMS 659C +
CYAN +
PMS 185C +
Black



Regulatory Operations

Label: 2010-36,39x71,23-204b
Current 1

Lacquer area: ■
Lacquerform: 20027-1

Ozempic 1 mg

Colour: PMS 280C +
PMS 3155C +
PMS 185C +
Black



DISETUJUI OLEH BPOM: 27/05/2024

ID: EREG100383VR12300006