Professional Information

SCHEDULING STATUS

S4

WARNING: RISK OF THYROID C-CELL TUMOURS

- **In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumours at clinically relevant exposures. It is unknown whether OZEMPIC causes thyroid C-cell tumours, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumours has not been determined *[see Warnings and special Precautions].***
- **OZEMPIC is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications (4)].* Counsel patients regarding the potential risk for MTC with the use of OZEMPIC and inform them of symptoms of thyroid tumours (e.g. a mass in the neck, dysphagia, dyspnoea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with OZEMPIC *[see Special warnings and precautions for use].***

1 NAME OF THE MEDICINE

Ozempic - Solution for injection in a pre-filled pen

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 1,34 mg of semaglutide (a human glucagon-like peptide-1 (GLP-1) receptor agonist produced in *Saccharomyces cerevisiae* by recombinant DNA technology), preserved with 5,50 mg/ml (0,55 % m/v) phenol.

Ozempic 0,25 mg and 0,5 mg/dose pen:

Each pre-filled pen contains 2 mg semaglutide in 1,5 ml solution

Ozempic 1 mg/dose pen:

Each pre-filled pen contains 4 mg semaglutide in 3 ml solution

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (injection).

Clear and colourless or almost colourless, isotonic solution;

pH=7.4.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ozempic is indicated:

- for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise
    - as monotherapy when metformin is considered inappropriate due to intolerance or contraindications.

- as combination therapy with oral anti-diabetic medicines (metformin, thiazoledinediones, sulphonylurea), basal insulin with or without metformin and pre-mix insulin.

- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease**.**

4.2 Posology and method of administration

Dosage

Ozempic starting dose is 0,25 mg once weekly. After 4 weeks, the dose should be increased to 0,5 mg once weekly. After at least 4 weeks with a dose of 0,5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control.

Ozempic dose 0,25 mg is not a therapeutic dose.

Ozempic can be used as monotherapy or as combination therapy with one or more antidiabetic medicines. See section *4.1 Therapeutic indications* for further information.

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

When Ozempic is added to existing sodium-glucose cotransporter 2 (SGLT2) inhibitor therapy, the current dose of SGLT2 inhibitor can be continued unchanged.

When Ozempic is added to existing therapy of a sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia (see *4.4 Special warnings and precautions for use*).

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

Special populations

Elderly (≥ 65 years old): No dose adjustment is required based on age.

Gender and Ethnicity:

No dose adjustment is required based on gender, age, race or ethnicity.

Patients with renal impairment:

No dose adjustment is required for patients with renal impairment. Experience with the use of Ozempic in patients with end-stage renal impairment is limited. Caution should be exercised when treating these patients with Ozempic.

Patients with hepatic impairment:

No dose adjustment is required for patients with hepatic impairment. Experience with the use of Ozempic in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with Ozempic.

Children and adolescents:

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

Method of administration

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

Ozempic is to be injected subcutaneously in the abdomen, in the thigh or in the upper arm. The injection site can be changed without dose adjustment.

Ozempic should not be administered intravenously or intramuscularly.

The day of weekly administration can be changed if necessary as long as the time between two doses is at least 2 days (> 48 hours).

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.

4.3 Contraindications

- Hypersensitivity to semaglutide or to any of the excipients listed under *2 QUALITATIVE AND QUANTITATIVE COMPOSITION.*
- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) (see 4.4 Special warnings and precautions for use.
- Pregnancy and lactation. Women who may become pregnant should use effective contraception while taking Ozempic (see 4.6 Fertility, pregnancy and lactation).

4.4 Special warnings and precautions for use

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

Ozempic is not a substitute for insulin.

Gastrointestinal effects

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

Acute pancreatitis

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

In the absence of other signs and symptoms of acute pancreatitis, elevations in pancreatic enzymes alone are not predictive of acute pancreatitis.

Hypoglycaemia

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

Diabetic retinopathy

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Long-term glycaemic control decreases the risk of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for worsening and treated according to clinical guidelines.

Heart failure

There is no therapeutic experience in patients with congestive heart failure New York Heart Association (NYHA) class IV.

Risk of Thyroid C-cell Tumours

In mice and rats, semaglutide caused a dose dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumours (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures. It is unknown whether Ozempic causes thyroid C-cell tumours, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumours has not been determined.

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist have been reported in the post marketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

Ozempic is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of Ozempic and inform them of symptoms of thyroid tumours e.g. mass in the neck, dysphaqia, dyspnoea, persistent hoarseness). Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

Hypersensitivity

Serious hypersensitivity reactions (e g anaphylaxis, angioedema) have been reported with GLP-1 receptor agonists such as Ozempic If hypersensitivity reactions occur, discontinue use of Ozempic; treat promptly per standard of care and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to Ozempic (see 4.3 Contraindications).

Effects on ability to drive and use machines

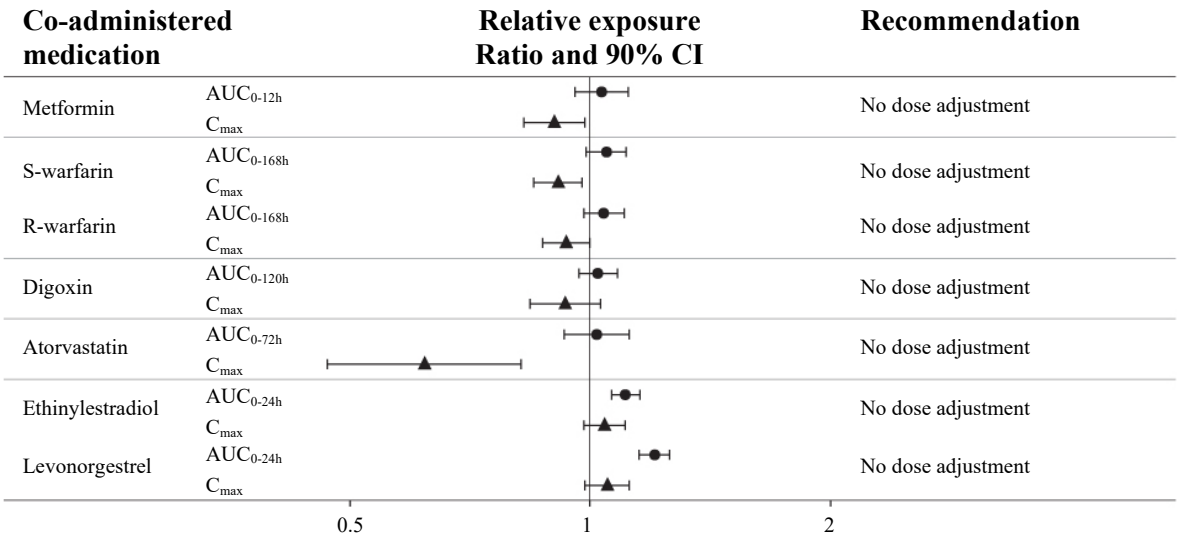
When it is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.

4.5 Interaction with other medicines and other forms of interaction

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

The delay of gastric emptying with Ozempic may influence the absorption of concomitantly administered oral medicines. The potential effect of Ozempic on the absorption of co-administered oral medicines was studied in trials at Ozempic 1 mg steady state exposure.

No clinically relevant interaction with Ozempic (*Figure 1*) was observed based on the evaluated medicines. Therefore, no dose adjustment is required when co-administered with Ozempic.



Relative exposure in terms of AUC and C_{max} for each medication when given with Ozempic® compared to without Ozempic®. Metformin and oral contraceptive drug ethinylestradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), digoxin and atorvastatin were assessed after a single dose.

Abbreviations: AUC: area under the curve. C_{max}: maximum concentration. CI: confidence interval.

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

4.6 Fertility, pregnancy and lactation

Ozempic is contraindicated during pregnancy and lactation (see 4.3 Contraindications).

Pregnancy

Studies in animals have shown reproductive toxicity. Semaglutide should not be used during pregnancy. The safety of Ozempic in

pregnant women has not been established. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life.

Women who may become pregnant should use effective contraception while taking Ozempic and for 2 months after stopping the medicine.

Lactation

It is unknown whether semaglutide is excreted in human milk. In lactating rats, semaglutide was excreted in milk. Women on treatment with Ozempic should not breastfeed their infants.

4.7 Effects on ability to drive and 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.

4.8 Undesirable effects

Summary of safety profile

In 8 phase 3a trials, 4,792 patients were exposed to Ozempic alone or in combination with other glucose lowering medicines. The duration of the treatment ranged from 30 weeks to 2 years. The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea, diarrhoea and vomiting.

Tabulated list of adverse reactions

Table 1 lists adverse reactions identified in phase 3a trials in patients with type 2 diabetes (further described in section Description of selected adverse reactions). The frequencies of the adverse reactions are based on a pool of the phase 3a trials excluding the cardiovascular outcomes trial.

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

Table 1: Side effects from controlled phase 3a trials

MedDRA system organ class	Very common	Common	Uncommon	Rare
Immune-system disorders			Hypersensitivity[c]	Anaphylactic reaction
Metabolism and nutrition disorders	Hypoglycaemia[a] when used with insulin or sulfonylurea	Hypoglycaemia[a] when used with other OADs Decreased appetite		
Nervous system disorders		Dizziness	Dysgeusia	
Eye disorders		Diabetic retinopathy complications[b]		

Cardiac disorders			Increased heart rate	
Gastrointestinal disorders	Nausea Diarrhoea	Vomiting Abdominal pain Abdominal distension Constipation Dyspepsia Gastritis Gastro-oesophageal reflux disease Eructation Flatulence	Acute pancreatitis	
Hepatobiliary disorders		Cholelithiasis		
General disorders and administration site conditions		Fatigue	Injection site reactions	
Investigations		Increased lipase Increased amylase Weight decreased		

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

2-year cardiovascular outcomes and safety trial

In a high cardiovascular risk population the adverse reaction profile was similar to that seen in the other phase 3a trials.

Description of selected adverse reactions

Hypoglycaemia

One episode of severe hypoglycaemia was observed when Ozempic was used as monotherapy. Severe hypoglycaemia was primarily observed when Ozempic was used with a sulfonylurea (1,2 % of subjects, 0,03 events/patient year) or insulin (1,5 % of subjects, 0,02 events/patient year). Few severe episodes (0,1 % of subjects, 0,001 events/patient year) were observed with Ozempic in combination with oral antidiabetics other than sulfonylureas.

Gastrointestinal adverse reactions

Nausea occurred in 17,0 % and 19,9 % patients when treated with Ozempic 0.5 mg and 1 mg respectively, diarrhoea in 12,2 % and 13,3 % and vomiting in 6,4 % and 8,4 %. Most events were mild to moderate in severity and of short duration. The events led to treatment discontinuation in 3,9 % and 5,9 % of subjects. The events were most frequently reported during the first months on treatment.

Diabetic retinopathy complications

In a 2-year clinical trial involving 3,297 patients with type 2 diabetes and high cardiovascular risk, long duration of diabetes and poorly controlled blood glucose, adjudicated events of diabetic retinopathy occurred in more patients treated with Ozempic (3,0 %) compared to placebo (1,8 %). The absolute risk

increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline. In the patients that did not have a documented history of diabetic retinopathy the number of events were similar for Ozempic and placebo.

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 4.4 Special warnings and precautions for use).

Discontinuation due to an adverse event

The incidence of discontinuation of treatment due to adverse events was 8.7 % for patients treated with 1 mg of Ozempic. The most frequent adverse events leading to discontinuation were gastrointestinal.

4.9 Overdose

There is no specific antidote for overdose with Ozempic. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these

symptoms may be necessary, taking into account the long half-life of Ozempic of approximately 1 week.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Semaglutide reduces blood glucose through a mechanism where it stimulates insulin secretion and lowers glucagon secretion, both in a glucose-dependent manner.

Semaglutide reduces body weight and body fat mass through lowered energy intake. The mechanism involves an overall reduced appetite, which includes increased satiety and reduced hunger.

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

5.2 Pharmacokinetic properties

Semaglutide has pharmacokinetic properties compatible with once weekly administration, with an elimination half-life of approximately 1 week.

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 s.c. 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 s.c. administration of semaglutide in the abdomen, thigh, or upper arm. Absolute bioavailability of s.c semaglutide was 89 %.

Distribution

The mean volume of distribution of semaglutide following s.c. administration in patients with type 2 diabetes was approximately 12,5 L. Semaglutide was extensively bound to plasma albumin (> 99 %).

Metabolism/biotransformation

Semaglutide is metabolised through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

Elimination

The primary excretion routes of semaglutide related material were via the urine (53 %) and faeces (18,6 %). Approximately 3% of the dose was excreted as intact semaglutide via urine.

Clearance of semaglutide in patients with type 2 diabetes 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 populations

No dose adjustment of semaglutide is needed based on age, gender, race, ethnicity, body weight, or renal or hepatic impairment.

Renal impairment:

Renal impairment did not impact the pharmacokinetics of semaglutide in a clinically relevant manner. 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.

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.

Paediatrics:

Semaglutide has not been studied in paediatric patients.

A phase 3b trial (SUSTAIN 9) including 302 patients, was conducted to investigate the efficacy and safety of semaglutide as add-on to SGLT2 inhibitor treatment (with or without metformin or sulfonylurea) in subjects with type 2 diabetes mellitus.

SUSTAIN 9 – Ozempic vs. placebo as add-on to SGLT2 inhibitor with or without metformin or SU

In a 30-week double-blind placebo-controlled trial, 302 patients inadequately controlled with SGLT2 inhibitor with or without metformin or SU were randomised to Ozempic 1,0 mg once weekly or placebo.

Patients had a mean age of 57 years and a mean duration of type 2 diabetes of 9,7 years, 69 % were White, 4 % were Black or African-American and 24% were Asian. For

ethnicity, 7 % of patients (n=22) were Hispanic or Latino.

Mean BMI was 32 kg/m^2. Treatment with Ozempic 1,0 mg as add-on to SGLT2 inhibitors resulted in statistically superior reductions in HbA_{1c} and body weight after 30 weeks of treatment compared to placebo.

Table 2: Results at 30 weeks of Ozempic in combination with SGLT2 inhibitor with or without metformin or SU (SUSTAIN 9)

	Ozempic 1 mg	**Placebo**
Intent-to-Treat (ITT) Population (N)	151	151
HbA_{1c} (%)		
Baseline (mean)	8.0	8,1
Change from baseline 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[b]	18,7
Patients (%) achieving HbA_{1c} ≤ 6,5 %	56,1[b]	3,9
FPG (mmol/l)		
Baseline (mean)	9,1	8,9
Change from baseline at week 30	-2,2	0,0
Difference from placebo [95 % CI]	-2,2 [-2,6; -1,8][b]	-
Body weight (kg)		
Baseline (mean)	89,6	93,8
Change from baseline week 30	-4,7	-0,9
Difference from placebo [95 % CI]	-3,8 [-4,7; - 2,9][a]	-
Patients (%) achieving weight loss ≥5 %	49,9[b]	8,2
Patients (%) achieving weight loss ≥10 %	15,1[b]	1,4

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

[b]p <0.001 for treatment difference, unadjusted for multiplicity

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dihydrate

Propylene glycol

Hydrochloric acid

Sodium hydroxide

Water for injections

Ozempic contains less than 1 mmol sodium (23 mg (m/v)) per dose, i.e. essentially 'sodium-free'.

6.2 Incompatibilities

Substances added to Ozempic may cause degradation of semaglutide. Ozempic must not be mixed with other medicines, e.g. infusion fluids.

6.3 Shelf life

3 years.

In-use shelf life: 6 weeks.

After first use:

Store at or below 30 °C or in a refrigerator (between 2 °C to 8 °C).

Do not freeze Ozempic and do not use Ozempic if it has been frozen.

Keep the pen cap on when Ozempic pen is not in use in order to protect from light.

Ozempic should be protected from excessive heat and light.

Discard any unused portion after 42 days (6 weeks)

Do not use Ozempic after the expiry date which is stated on the pen label and carton i.e. after 'EXP'. The expiry date refers to the last day of that month.

6.4 Special precautions for storage

Before use:

Store in a refrigerator (between 2 °C to 8 °C). Keep away from the cooling element. Protect from light.

Do not freeze Ozempic and do not use Ozempic if it has been frozen.

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

6.5 Nature and contents of container

The primary packaging consists of a 1,5 ml or 3 ml glass (Type I glass) cartridge closed at the one end with a grey rubber plunger (chlorobutyl rubber) and at the other end with an aluminium cap with a cream laminate rubber disc (bromobutyl/polyisoprene) inserted.

The cartridge is assembled into a pre-filled multidose disposable pen made of polypropylene, polyoxymethylene polycarbonate and acrylonitrile butadiene styrene.

There are two presentations of the pre-filled pen for Ozempic:

- Ozempic 0,25 mg and 0,5 mg/dose pen: Contains 1,5 ml solution for injection. The pen is designed to deliver doses of 0,25 mg or 0,5 mg. This pen is intended to be used for dose escalation and maintenance treatment at the 0,5 mg dose.

  The pen is light blue when capped, with PMS cool gray 6C dose button, on remove of the cap the pen consists of PMS cool gray 6C cartridge holder with light blue housing, labelled with summit red label.

- Ozempic 1 mg/dose pen: Contains 3 ml solution for injection. The pen is designed to deliver doses of 1 mg only. This pen is to be used for maintenance treatment at the 1 mg dose only.

  The pen is light blue when capped, with PMS cool gray 6C dose button, on remove of the cap the pen consists of PMS cool gray 6C cartridge holder with light blue housing, labelled with petrol blue label.

The pen(s) is/are packed in carton box.

Pack sizes:

Ozempic 0,25 mg, 0,5 mg/dose pen:

1 x 1,5 ml pre-filled pen including 6 disposable NovoFine® Plus needles

Ozempic 1 mg/dose pen:

1 x 3 ml pre-filled pen including 4 disposable NovoFine® Plus needles

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.

Needles and other waste material should be disposed of in accordance with local requirements.

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 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.

For detailed instructions for use, see *Instructions on how to use Ozempic.*

7 HOLDER OF CERTIFICATE OF REGISTRATION

Novo Nordisk (Pty) Ltd

Marion Street Office Park

Block C1, 10 Marion Street

Sandton, 2196

8 REGISTRATION NUMBER(S)

53/21.13/0497

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07 July 2020

10 DATE OF REVISION OF THE TEXT

14 December 2021

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.

Do not use the pen without proper training from your doctor or nurse.

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.

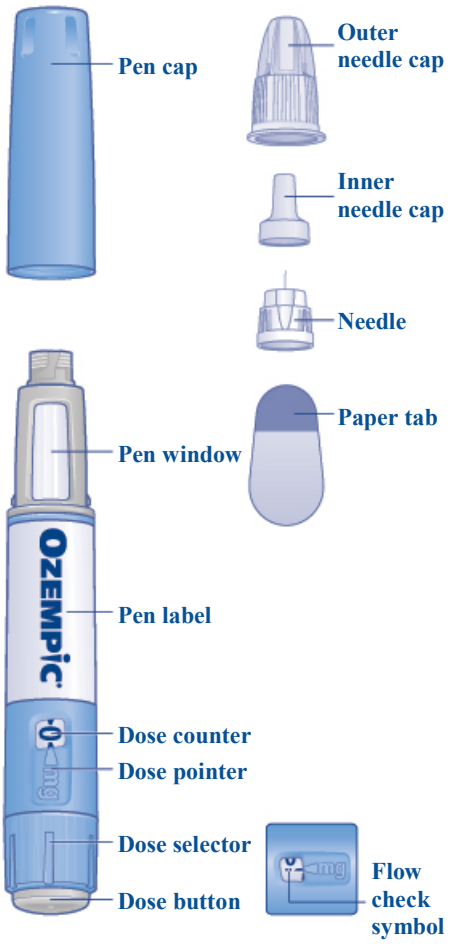
If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the Ozempic® pre-filled pen.

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. 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.

Needles are medical devices.

Ozempic® pre-filled pen and needle (example)



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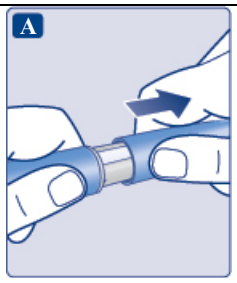
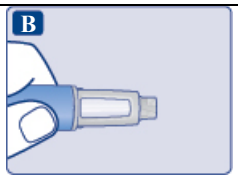
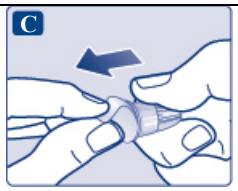
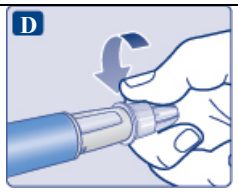
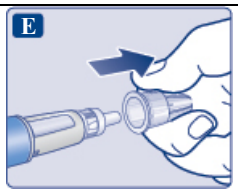
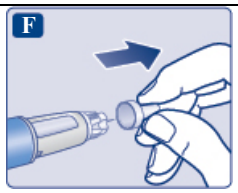
Pay special attention to these notes, as they are important for safe use of the pen.

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.**	
• **Push the needle straight onto the pen. Turn until it is on tight.**	
• **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’.

Do not attach a new needle to your pen until you are ready to take your injection.

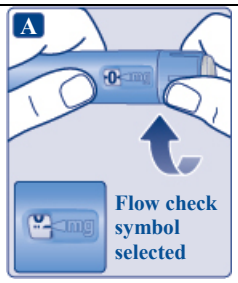
⚠

This may prevent blocked needles, contamination, infection and inaccurate dosing.

⚠ **Never use a bent or damaged needle.**

2. Check the flow

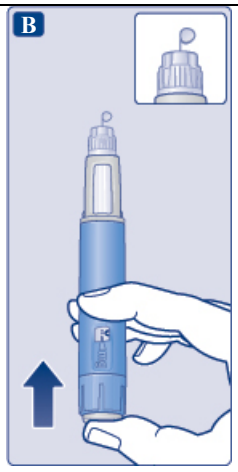
- **Before your first injection with each new pen**, **check the flow.** If your pen is already in use, go to step 3 ‘Select your dose’.



- 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' up to 6 times. If there is still no drop, change the needle and repeat step 2 'Check the flow' once more.

If a drop still does not appear, dispose of the pen and use a new one.

⚠

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.**

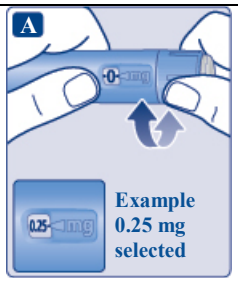
If you do not check the flow before your first injection with each new pen, you may not get the prescribed dose and the intended effect of Ozempic®.

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.

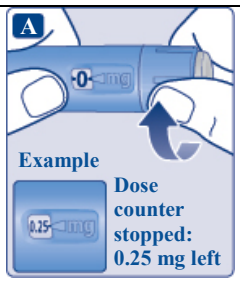
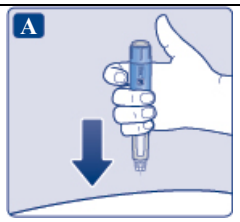
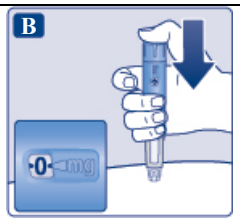
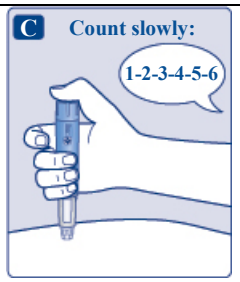
The dose selector clicks differently when turned forwards, backwards or past the number of mg left. Do not count the pen clicks.

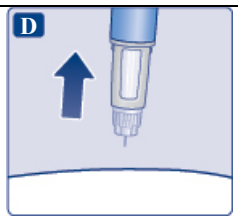
⚠

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.	
⚠	
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 until the dose counter shows 0.** The 0 must line up with the dose pointer. You may then hear or feel a click.	
• **Keep the needle in your skin** after the dose counter has returned to 0 and **count slowly to 6.** • 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**. If blood appears at the injection site, press lightly. Do not rub the area.	
You may see a drop of solution at the needle tip after injecting. This is normal and does not affect your dose.	

⚠

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.

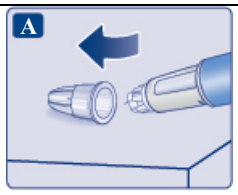
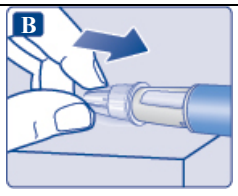
– In this case, you have **not** received any medicine – even though the dose counter has moved from the original dose that you have set.

How to handle a blocked needle

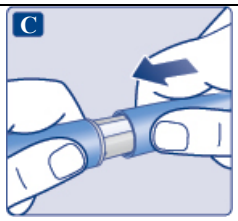
Change the needle as described in step 5 ‘After your injection’ and repeat all steps starting with step 1 ‘Prepare your pen with a new needle’. Make sure you select the full dose you need.

Never touch the dose counter when you inject. This can interrupt the injection.

5. After your injection

• **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.	

- **Put the pen cap on** your pen after each use to protect the solution from light.



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.

When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities.

⚠

⚠

This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.

⚠

- 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.** If necessary, clean it 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.

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

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

Do not use the pen without proper training from your doctor or nurse.

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

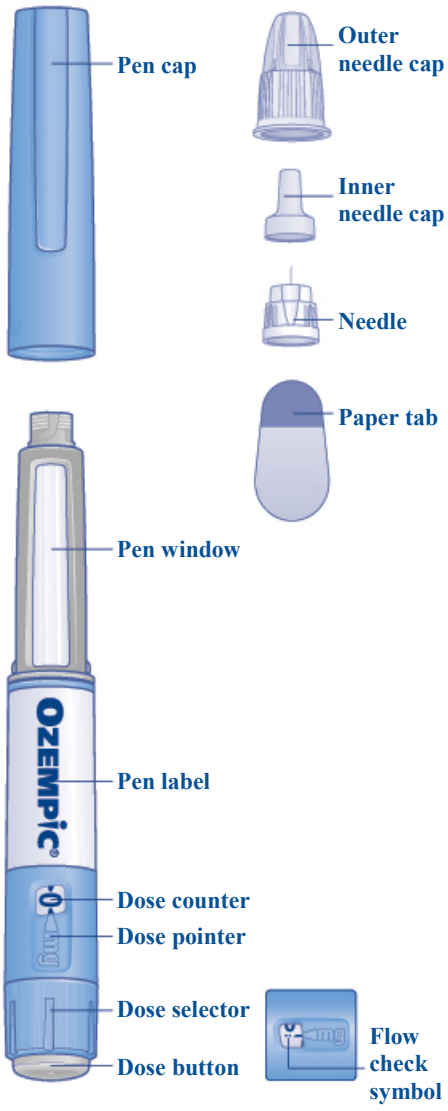
If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the Ozempic® pre-filled pen.

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. 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.

Needles are medical devices.

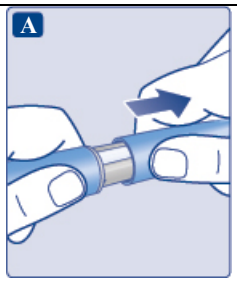
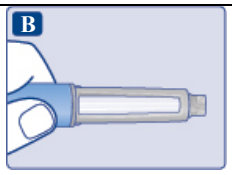
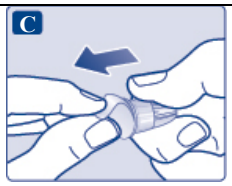
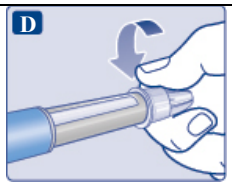
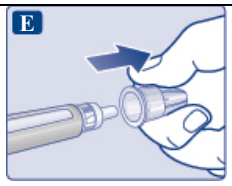
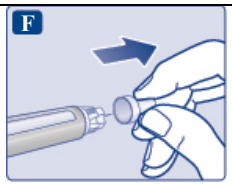
Ozempic® pre-filled pen and needle (example)



⚠

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

1. Prepare your pen with a new needle

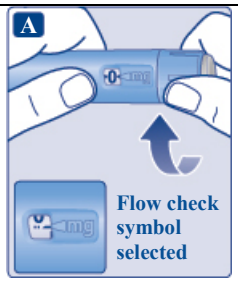
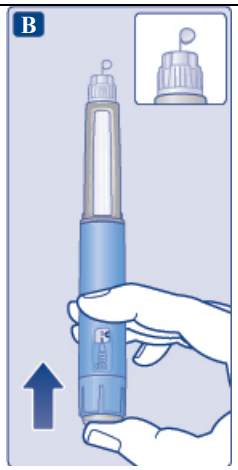
• **Check the name and coloured label** of your pen to make sure that it contains Ozempic® 1 mg/dose. This is especially important if you take more than one type of injectable medicine. Using the wrong medicine could be harmful to your health. • **Pull off the pen cap.**	
• **Check that the solution 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.**	
• **Push the needle straight onto the pen. Turn until it is on tight.**	
• **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’.	

Do not attach a new needle to your pen until you are ready to take your injection.	

⚠ This may prevent blocked needles, contamination, infection and inaccurate dosing.

⚠ **Never use a bent or damaged needle.**

2. Check the flow

• **Before your first injection with each new pen, check the flow.** If your pen is already in use, go to step 3 'Select your dose'.	
• 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' up to 6 times. If there is still no drop, change the needle and repeat step 2 'Check the flow' once more.

If a drop still does not appear, dispose of the pen and use a new one.

⚠ 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.

⚠

Do not count the pen clicks.

Only doses of 1 mg must be selected with the dose selector. 1 mg must line up precisely with the dose pointer to ensure that you get a correct dose.

How much solution is left

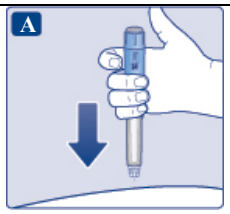
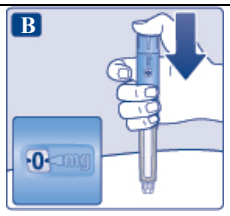
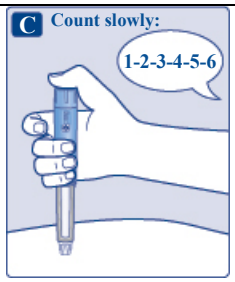
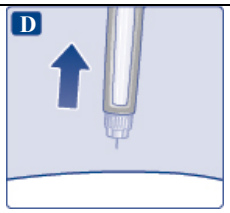
- **To see how much solution is left,** use the dose counter: Turn the dose selector until the **dose counter stops.**

  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.

⚠ 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 until the dose counter shows 0.** The 0 must line up with the dose pointer. You may then hear or feel a click.	
• **Keep the needle in your** skin after the dose counter has returned to 0 and **count slowly to 6.** • 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.** If blood appears at the injection site, press lightly. Do not rub the area.	

You may see a drop of solution at the needle tip after injecting. This is normal and does not affect your dose.

⚠

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.

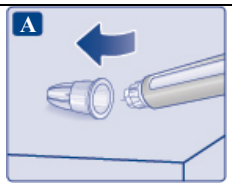
How to handle a blocked needle

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.

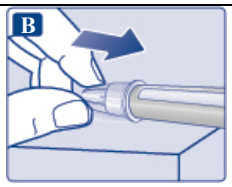
Never touch the dose counter when you inject. This can interrupt the injection.

5. After your injection

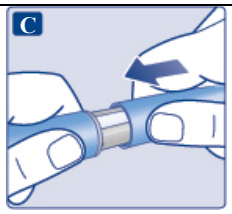
- **Lead the needle tip into the outer needle cap** on a flat surface without touching the needle or the outer needle cap.



- Once the needle is covered, **carefully push the outer needle cap completely on.**
- **Unscrew the needle** and dispose of it carefully.



- **Put the pen cap on** your pen after each use to protect the solution from light.



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.

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.

⚠

- 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.** If necessary, clean it 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.