PROFESSIONAL INFORMATION

S4 Saxenda®

6 mg/ml, Liraglutide, Solution for Injection

Scheduling status

S4

Proprietary name and dosage form

Saxenda®, solution for injection in pre-filled pen.

Composition

One ml of solution contains 6 mg of liraglutide (produced by recombinant DNA technology in *Saccharomyces cerevisiae*) and phenol 0,55 % m/v as the preservative.

Excipients
Disodium phosphate dihydrate
Propylene glycol
Sodium hydroxide
Hydrochloric acid
Water for injections

Pharmacological classification

A 21.13 Other hormones

Pharmacological action

Pharmacodynamic properties

Mechanism of action

Liraglutide is a human Glucagon-Like Peptide-1 (GLP-1) analogue with 97 % homology to human GLP-1 that binds to and activates the GLP-1 receptor.

The GLP-1 receptor is the target for native GLP-1, an endogenous incretin hormone that potentiates glucose-dependent insulin secretion from the pancreatic beta cells. Unlike native GLP-1, liraglutide has a pharmacokinetic and pharmacodynamic profile in humans, suitable for once daily administration.

Following subcutaneous administration, the protracted action profile is based on three mechanisms: self-association, which results in slow absorption, and binding to albumin and enzymatic stability towards the DPP-IV and NEP enzymes resulting in a long plasma half-life.

Liraglutide action is mediated via a specific interaction with GLP-1 receptors, leading to an increase in cAMP. Liraglutide stimulates insulin secretion in a glucose-dependent manner and improves beta-cell function. Simultaneously, liraglutide lowers inappropriately high glucagon secretion, also in a glucose-dependent manner. Thus, when blood glucose is high, insulin secretion is stimulated and glucagon secretion is inhibited. Conversely, during hypoglycaemia liraglutide diminishes insulin secretion and does not impair glucagon secretion. The mechanism of blood glucose lowering also involves a delay in gastric emptying.

GLP-1 is a physiological regulator of appetite and food intake and GLP-1R is present in several areas of the brain involved in appetite regulation. In animal studies, peripheral administration of liraglutide led to uptake in specific brain regions including the hypothalamus, where liraglutide, via specific activation of the GLP-1R, increased satiety and decreased hunger signals, thereby leading to lower body weight. Liraglutide reduces body weight and body fat mass. Body weight is lowered through decreased food intake. Liraglutide does not increase 24-hour energy expenditure.

Liraglutide regulates appetite by increasing feelings of fullness and satiety, while lowering feelings of hunger and prospective food consumption.

Pharmacodynamic effects

Liraglutide has 24-hour duration of action and improves glycaemic control by lowering fasting and postprandial blood glucose.

Fasting and postprandial glucose, insulin and glucagon concentrations were assessed before and up to five hours after a standardised meal. Compared to placebo, liraglutide reduced fasting glucose and postprandial glucose ($AUC_{0\text{-}60\ min}$) in the first hour after the meal, and also reduced 5-hour glucose AUC and incremental glucose ($AUC_{0\text{-}300\ min}$). In addition, liraglutide decreased postprandial glucagon ($AUC_{0\text{-}300\ min}$), postprandial insulin ($AUC_{0\text{-}60\ min}$) and incremental insulin ($iAUC_{0\text{-}60\ min}$) after the meal compared with placebo.

Fasting and incremental glucose and insulin concentrations were also assessed during a 75 g oral glucose tolerance test (OGTT) before and after one year of treatment in 3731 overweight and obese patients with and without pre-diabetes. Compared to placebo, liraglutide reduced fasting and incremental glucose concentrations. The effect was more pronounced in patients with pre-diabetes. In addition, liraglutide reduced fasting insulin and increased incremental insulin concentrations compared to placebo.

Effects on fasting and postprandial glucose increment in overweight and obese patients with type 2 diabetes mellitus
Liraglutide reduced fasting glucose and mean postprandial glucose increment (90 minutes after the meal, average over 3 daily meals), compared to placebo.

Pharmacokinetic properties

Liraglutide is stable against metabolic degradation and has a plasma half-life of 13 hours after subcutaneous administration. The pharmacokinetic profile of liraglutide, which makes it suitable for once daily administration, is a result of self-association that delays absorption, plasma protein binding and stability against metabolic degradation by dipeptidyl peptidase-4 (DPP-4) and neutral endopeptidase (NEP).

Absorption
The absorption of liraglutide following subcutaneous administration was slow, reaching maximum concentration approximately 11 hours post dosing. The average liraglutide steady state concentration ($AUC_{\tau/24}$) reached approximately 31 nmol/l in obese (BMI 30 - 40 kg/m^2) subjects following administration of liraglutide 3,0 mg. Liraglutide exposure increased proportionally with dose in the dose range of 0,6 mg to 3,0 mg.

Absolute bioavailability of liraglutide following subcutaneous administration is approximately 55 %.

Distribution
The mean apparent volume of distribution after subcutaneous administration of liraglutide 3,0 mg is 20 - 25 l (for a person weighing approximately 100 kg). Liraglutide is extensively bound to plasma protein (> 98 %).

Metabolism/biotransformation
During 24 hours following administration of a single [3H]-liraglutide dose to healthy subjects, the major component in plasma was intact liraglutide. Two minor plasma metabolites were detected (≤ 9 % and ≤ 5 % of total plasma radioactivity exposure).

Elimination
Liraglutide is endogenously metabolised in a similar manner to large proteins without a specific organ as major route of elimination. Following a [3H]-liraglutide dose, intact liraglutide was not detected in urine or faeces.

Only a minor part of the administered radioactivity was excreted as liraglutide-related metabolites in urine or faeces (6 % and 5 %, respectively).

The urine and faeces radioactivity was mainly excreted during the first 6 - 8 days, and corresponded to three minor metabolites, respectively.

The apparent clearance following *s.c.* administration of liraglutide 3,0 mg is approximately 0,9 – 1,4 l/h with an elimination half-life of approximately 13 hours.

Special populations

Elderly
No dosage adjustment is required based on age. Age had no clinically relevant effect on the pharmacokinetics of liraglutide 3,0 mg based on a population pharmacokinetic analysis that included overweight and obese patients (18 to 82 years).

Body weight
The exposure of liraglutide decreases with an increase in baseline body weight. The 3,0 mg daily dose of liraglutide provided adequate systemic exposures over the body weight range of 60 - 234 kg evaluated for exposure response in the clinical trial. Liraglutide exposure was not studied in subjects with body weight > 234 kg.

Hepatic impairment
The pharmacokinetics of liraglutide was evaluated in patients with varying degree of hepatic impairment in a single-dose trial (0,75 mg). Liraglutide exposure was decreased by 23 % and 13 % in patients with mild and moderate hepatic impairment, respectively, compared to healthy subjects. Exposure was significantly lower (44 %) in patients with severe hepatic impairment (Child Pugh score > 9).

Renal impairment
Liraglutide exposure was reduced in patients with renal impairment compared to individuals with normal renal function in a single-dose trial (0.75 mg). Liraglutide exposure was lowered by 33 %, 14 %, 27 % and 26 %, in patients with mild (creatinine clearance, CrCl 50 - 80 ml/min), moderate (CrCl 30 - 50 ml/min), and severe (CrCl < 30 ml/min) renal impairment and in end-stage renal disease requiring dialysis, respectively.

Paediatrics
Liraglutide has not been studied in paediatric patients.

Indications

Saxenda® is indicated as an adjunct to a reduced-calorie diet and increased physical activity for medically supervised chronic weight management programme in adult patients with an initial Body Mass Index (BMI) of:

- ≥ 30 kg/m^2 (obese),
  or
- ≥ 27 kg/m^2 to < 30 kg/m^2 (overweight) in the presence of at least one weight related comorbidity such as dysglycaemia (pre-diabetes and type 2 diabetes mellitus), hypertension, dyslipidaemia, or obstructive sleep apnoea.

Contra-indications

- Hypersensitivity to liraglutide or to any of the excipients listed under Composition.
- Pregnancy and lactation (*see* Pregnancy and Lactation).

Warnings and special precautions

Saxenda® must not be used as a substitute for insulin.
There is limited experience in patients with congestive heart failure New York Heart Association (NYHA) class I - II and Saxenda® should therefore be used with caution. There is no experience in patients with congestive heart failure NYHA class III - IV and Saxenda® is therefore not recommended in these patients.

The safety and efficacy of Saxenda® have not been established in patients:

- Treated with other products for weight management,
- With obesity secondary to endocrinological or eating disorders or to treatment with medicinal products that may cause weight gain,
- With severe renal impairment,
- With severe hepatic impairment.

Use in these patients is not recommended.

There is limited experience in patients with inflammatory bowel disease and diabetic gastroparesis. Use of Saxenda® is not recommended in these patients since it is associated with transient gastrointestinal adverse reactions, including nausea, vomiting and diarrhoea.

Pancreatitis
Use of GLP-1 receptor agonists such as Saxenda® has been associated with the risk of developing acute pancreatitis. There have been reported events of acute pancreatitis with Saxenda®. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Saxenda® should be discontinued; if acute pancreatitis is confirmed, Saxenda® should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Cholelithiasis and cholecystitis
In clinical trials, a higher rate of cholelithiasis and cholecystitis was observed in patients treated with Saxenda® than in patients on placebo. Cholelithiasis and cholecystitis may lead to hospitalisation and cholecystectomy. Patients should be informed of the characteristic symptoms of cholelithiasis and cholecystitis.

Thyroid disease
In clinical trials in type 2 diabetes, thyroid adverse events, including increased blood calcitonin, goitre and thyroid neoplasm have been reported in particular in patients with pre-existing thyroid disease. Saxenda® should therefore be used with caution in patients with thyroid disease.

Heart rate
An increase in heart rate was observed in clinical trials.
Heart rate should be monitored at regular intervals consistent with usual clinical practice. Patients should be informed of the symptoms of increased heart rate (palpitations or feelings of a racing heartbeat while at rest). For patients who experience a clinically relevant sustained increase in resting heart rate, treatment with Saxenda® should be discontinued.

Dehydration
Signs and symptoms of dehydration, including renal impairment and acute renal failure have been reported in patients treated with GLP-1 receptor agonists such as Saxenda®. Patients treated with Saxenda® should be advised of the potential risk of dehydration in relation to gastrointestinal side effects and take precautions to avoid fluid depletion.

Hypoglycaemia in overweight or obese patients with type 2 diabetes mellitus

Patients with type 2 diabetes receiving Saxenda® in combination with a sulphonylurea have an increased risk of hypoglycaemia. The risk of hypoglycaemia may be lowered by a reduction in the dose of sulphonylurea. Blood glucose levels should be carefully monitored during treatment with Saxenda® in patients with type 2 diabetes.

The addition of Saxenda® in patients treated with insulin has not been evaluated.

Effects on ability to drive and use machines

Dizziness may impair the ability to drive and use machines.

Interactions

In vitro assessment of interaction

Saxenda® has shown very low potential to be involved in pharmacokinetic interactions related to cytochrome P450 (CYP) and plasma protein binding.

In vivo assessment of interaction
The delay of gastric emptying with Saxenda® may influence absorption of concomitantly administered oral medicines. Interaction studies did not show any clinically relevant delay of absorption and therefore no dose adjustment is required.

Interaction studies have been performed with 1.8 mg liraglutide. The effect on rate of gastric emptying was equivalent between liraglutide 1.8 mg and 3 mg, (paracetamol $AUC_{0\text{-}300\ min}$). Few patients treated with liraglutide reported at least one episode of severe diarrhoea. Diarrhoea may affect the absorption of concomitant oral medicines.

Warfarin and other coumarin derivatives
No interaction study has been performed. A clinically relevant interaction with active substances with poor solubility or narrow therapeutic index such as warfarin cannot be excluded. Upon initiation of Saxenda® treatment in patients,on warfarin or other coumarin derivatives more frequent monitoring of INR (International Normalised Ratio) is recommended.

Paracetamol (Acetaminophen)
Saxenda® did not change the overall exposure of paracetamol following a single dose of 1,000 mg. Paracetamol C_{max} was decreased by 31 % and median t_{max} was delayed up to 15 min. No dose adjustment for concomitant use of paracetamol is required.

Atorvastatin
Saxenda® did not change the overall exposure of atorvastatin following single dose administration of atorvastatin 40 mg. Therefore, no dose adjustment of atorvastatin is required when given with Saxenda®. Atorvastatin C_{max} was decreased by 38 % and median t_{max} was delayed from 1 h to 3 h with liraglutide.

Griseofulvin
Saxenda® did not change the overall exposure of griseofulvin following administration of a single dose of griseofulvin 500 mg. Griseofulvin C_{max} increased by 37 % while median t_{max} did not change. Dose adjustments of griseofulvin and other compounds with low solubility and high permeability are not required.

Digoxin
A single dose administration of digoxin 1 mg with liraglutide resulted in a reduction of digoxin AUC by 16 %; C_{max} decreased by 31 %. Digoxin median t_{max} was delayed from 1 h to 1,5 h. No dose adjustment of digoxin is required based on these results.

Lisinopril
A single dose administration of lisinopril 20 mg with liraglutide resulted in a reduction of lisinopril AUC by 15 %; C_{max} decreased by 27 %. Lisinopril median t_{max} was delayed from 6 h to 8 h with liraglutide. No dose adjustment of lisinopril is required based on these results.

Oral contraceptives
Liraglutide lowered ethinylestradiol and levonorgestrel C_{max} by 12 % and 13 %, respectively, following administration of a single dose of an oral contraceptive product. t_{max} was delayed by 1,5 h with liraglutide for both compounds. There was no clinically relevant effect on the overall exposure of either ethinylestradiol or levonorgestrel. The contraceptive effect is therefore anticipated to be unaffected when co-administered with Saxenda®

Pregnancy and Lactation

The safety of Saxenda® in pregnancy and lactation has not been established.

Saxenda® should not be used during pregnancy and lactation (*see* Contraindications).
If a patient wishes to become pregnant, or pregnancy occurs, treatment with Saxenda® should be discontinued.

Dosage and directions for use

The starting dose is 0,6 mg once daily. The dose should be increased to 3.0 mg once daily in increments of 0,6 mg with at least one week intervals to improve gastro-intestinal tolerability (*see Table 1*). If escalation to the next dose step is not tolerated for two consecutive weeks, consider discontinuing treatment. Daily doses higher than 3,0 mg are not recommended.

Table 1 Dose escalation schedule

	Dose	Weeks
Dose escalation 4 weeks	0,6 mg	1
	1,2 mg	1
	1,8 mg	1
	2,4 mg	1
Maintenance dose	**3,0 mg**	

Treatment with Saxenda® should be discontinued after 12 weeks on the 3,0 mg/day dose if a patient has not lost at least 5 % of the initial body weight. The need for continued treatment should be re-evaluated annually.

Patients with type 2 diabetes mellitus
Saxenda® should not be used in combination with another GLP-1 receptor agonist. When initiating Saxenda®, consider reducing the dose of concomitantly administered insulin or insulin secretagogues (such as sulfonylureas) to reduce the risk of hypoglycaemia.

Special populations

Elderly patients (≥ 65 years old)

No dose adjustment is required based on age. Due to limited experience in patients ≥ 75 years of age, Saxenda® should be used with caution in these patients.

Patients with renal impairment
No dose adjustment is required for patients with mild or moderate renal impairment (creatinine clearance ≥ 30 ml/min). There is limited experience in patients with severe renal impairment (creatinine clearance < 30 ml/min).

Saxenda® is currently not recommended for use in patients with severe renal impairment including patients with end-stage renal disease (*see section* Special population under Pharmacokinetic properties).

Patients with hepatic impairment
No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Saxenda® is not recommended for use in patients with severe hepatic impairment and should be used cautiously in patients with mild or moderate hepatic impairment (*see section* Special population under Pharmacokinetic properties).

Paediatric population
Saxenda® is not recommended for use in children below 18 years of age due to lack of data.

Method of administration
Saxenda® is for subcutaneous use only. It must not be administered intravenously or intramuscularly.

Saxenda® is administered once daily at any time, independent of meals. It should be injected in the abdomen, thigh or upper arm. The injection site and timing can be changed without dose adjustment. However, it is preferable that Saxenda® is injected around the same time of the day,

when the most convenient time of the day has been chosen. *For instructions for handling and how to administer Saxenda®* solution for injection in pre-filled pen refer to user instructions at the end of the package insert.

Missed dose
If a dose is missed within 12 hours from when it is usually taken, the patient should take the dose as soon as possible. If there is less than 12 hours to the next dose, the patient should not take the missed dose and resume the once-daily regimen with the next scheduled dose. An extra dose or increase in dose should not be taken to make up for the missed dose.

Side-effects

The clinical development programme for Saxenda® consists of 5 completed clinical trials that enrolled 5813 obese patients or overweight patients with at least one weight-related co-morbidity.

Overall, gastrointestinal reactions were the most frequently reported adverse reactions during treatment with Saxenda® (see section 'Description of selected side effects' below).

Table 2 lists adverse reactions reported in long term phase 3 and phase 2 controlled trials. Adverse reactions associated with Saxenda® are listed by body system and frequency. Frequency categories 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); very rare (< 1/10,000).

Table 2: Adverse reactions reported in phase 2 and phase 3 controlled trials

System organ classes	**Very common**	**Common**	**Uncommon**	**Rare**
Immune system disorders				Anaphylactic reaction
Metabolism and nutrition disorders		Hypoglycaemia*	Dehydration	
Psychiatric disorders		Insomnia		
Nervous system		Dizziness Dysgeusia		
Cardiac disorders			Tachycardia	
Gastrointestinal disorders	Nausea Vomiting Diarrhoea Constipation	Dry mouth Dyspepsia Gastritis Gastro-oesophageal reflux disease Abdominal pain upper Flatulence Eructation Abdominal Distension	Pancreatitis	
Hepatobiliary disorders		Cholelithiasis	Cholecystitis	
Skin and subcutaneous tissue disorders			Urticaria	

Renal and urinary disorders				Acute renal failure Renal impairment
General disorders and administration site conditions		Injection site reactions Asthenia Fatigue	Malaise	

**Hypoglycaemia (based on self-reported symptoms by patients and not confirmed by blood glucose measurements) reported in patients without type 2 diabetes mellitus treated with Saxenda® in combination with diet and exercise. Please see section 'Description of selected side effects' for further information.*

Description of selected side effects

Hypoglycaemia in patients without type 2 diabetes mellitus
In clinical trials in overweight or obese patients without type 2 diabetes mellitus treated with Saxenda® in combination with diet and exercise no severe hypoglycaemic events (requiring third party assistance) were reported. Symptoms of hypoglycaemic events were reported by 1,6 % of patients treated with Saxenda® and 1,1 % of patients treated with placebo.

Hypoglycaemia in patients with type 2 diabetes mellitus
In a clinical trial in overweight or obese patients with type 2 diabetes mellitus treated with Saxenda® in combination with diet and exercise, severe hypoglycaemia (requiring third party assistance) was reported by 0,7 % of patients treated with Saxenda® and only in patients concomitantly treated with sulfonylurea. In these patients documented symptomatic hypoglycaemia (defined as plasma glucose ≤ 3,9 mmol/l accompanied by symptoms) was reported by 43,6 % of patients treated with Saxenda® and in 27,3 % of patients treated with placebo. Among patients not concomitantly treated with sulfonylurea, 15,7 % of patients treated with Saxenda® and 7,6 % of patients treated with placebo reported documented symptomatic hypoglycaemic events.

Gastrointestinal adverse reactions
The reactions usually occurred during the first weeks of treatment and diminished within a few days or weeks on continued treatment. Patients ≥ 65 years of age may experience more gastrointestinal effects when treated with Saxenda®. Patients with mild or moderate renal impairment (creatinine clearance ≥ 30 ml/min) may experience more gastrointestinal effects when treated with Saxenda®.

Allergic reactions
Cases of anaphylactic reactions with symptoms such as hypotension, palpitations, dyspnoea, or oedema have been reported with marketed use of liraglutide. Anaphylactic reactions may potentially be life threatening.

Tachycardia
In clinical trials tachycardia was reported in 0,6 % of patients treated with Saxenda® and in 0,1 % of patients treated with placebo. The majority resolved during continued treatment with Saxenda®.

Known symptoms of overdosage and particulars of its treatment

With overdose, the patients reported severe nausea, vomiting and diarrhoea, but recovered without complications. None of the patients reported severe hypoglycaemia.

In the event of overdosage, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

Identification

Saxenda is a clear, colourless or almost colourless, isotonic solution, pH = 8.15

Presentation

3 ml solution in a cartridge made of colourless type 1 glass with a red rubber plunger (bromobutyl) and closed with a cream colour rubber stopper (bromobutyl/polyisoprene). The cartridge is contained in a pre-filled multidose disposable pen made of polypropylene, polyacetal, polycarbonate and acrylonitrile butadiene styrene. Each pen is able to deliver doses of 0,6 mg, 1,2 mg,1,8 mg, 2,4 mg and 3,0 mg.

Each pen is designed to be used with NovoFine® or NovoTwist® disposable needles of a length of 4 – 8 mm and a thickness of 30 – 32G.

The pen(s) is/are packed in hard card board paper
Pack sizes of 1, 3 or 5 pre-filled pens.

Not all pack sizes may be marketed.

Storage instructions

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Store away from the freezer compartment.

After first use: Store at or below 30 °C or store in a refrigerator (2 °C – 8 °C) for 30 days (1 month).

Discard any unused portion after 30 days.

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

Keep out of reach of children.

Registration number

50/21.13/1091

Name and business address of the holder of the certificate of registration

Novo Nordisk (Pty) Ltd
150 Rivonia Road
10 Marion Street Office Park
Building C1
Sandton, Johannesburg
2196

Date of publication of the professional information

Date on the registration certificated: 31 March 2020

Date of the most recently revised professional information as approved by SAHPRA: N/A

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Instructions on how to use Saxenda®, 6 mg/ml, solution for injection in pre-filled pen

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

Do not use the pen without proper training from your doctor; pharmacist or other healthcare professional.

Start by checking your pen to **make sure that it contains Saxenda® 6 mg/ml,** 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 Saxenda® pre-filled pen.

Your pen is a pre-filled dial-a-dose pen. It contains 18 mg of liraglutide, and delivers doses of 0,6 mg, 1,2 mg, 1,8 mg, 2,4 mg and 3,0 mg.

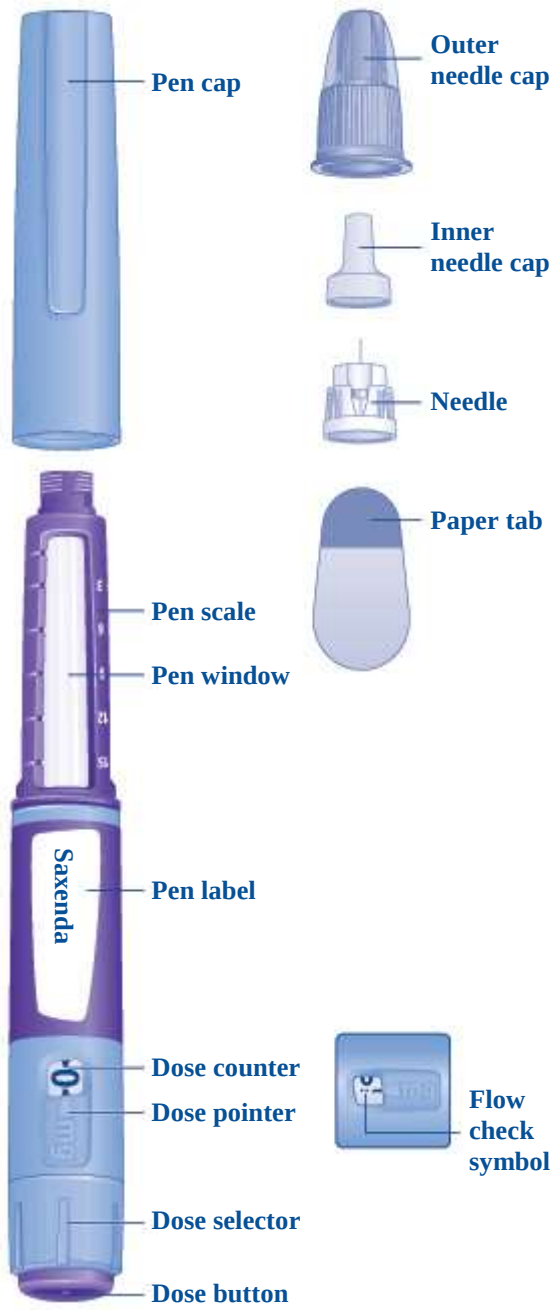
Your pen is designed to be used with NovoFine® or NovoTwist® disposable needles of a length of 4 – 8 mm and a thickness of 30 – 32G.

Needles are not included in the pack.

⚠ Important information

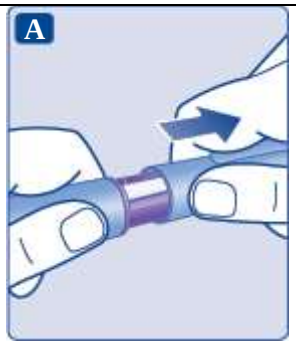
Pay special attention to these notes as they are important for safe use of the pen.

Saxenda pre-filled pen and needle (example)

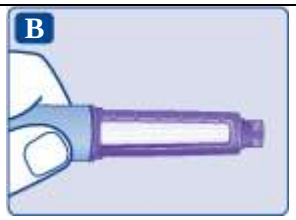


1. Prepare your pen with a new needle

- **Check the name and coloured label** of your pen, to make sure that it contains Saxenda®. 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, do not use the pen.



- **Take a new needle,** and 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 use.** 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.

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.**

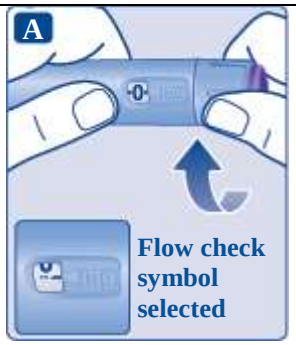
This may prevent blocked needles, contamination, infection and inaccurate dosing.

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

2 Check the flow

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’.
- Turn the dose selector **until the dose counter shows the flow check symbol** (▪▪ ▬).



- 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.

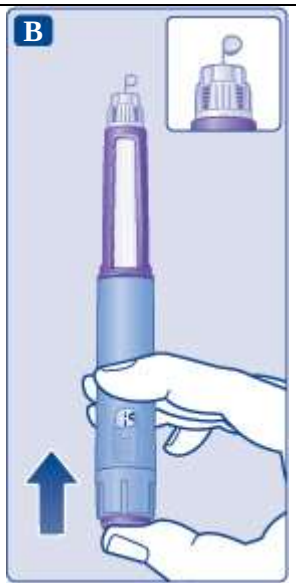
If no drop appears, repeat step 2 ‘Check the flow’ up to 6 times. If there is still no drop, change the needle and repeat step 2 ‘Check the flow’ once more.

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

⚠ **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 Saxenda®.



3 Select your dose

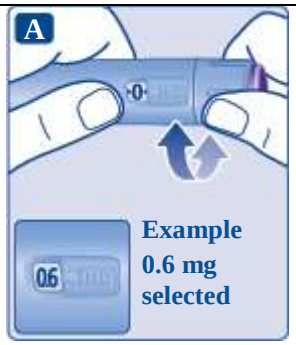
- **Turn the dose selector until the dose counter shows your dose (0,6 mg, 1,2 mg, 1,8 mg, 2,4 mg or 3,0 mg).**

If you select the wrong dose, you can turn the dose selector forward or backwards to the correct dose.

The pen can dial up to a maximum of 3,0 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 3.0 mg per dose. When your pen contains less than 3.0 mg the dose counter stops before 3.0 is shown.



The dose selector clicks differently when turned forward, 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.

Do not use the pen scale. It only shows approximately how much solution is left in your pen.

Only doses of 0,6 mg, 1,2 mg, 1,8 mg, 2,4 mg or 3,0 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.

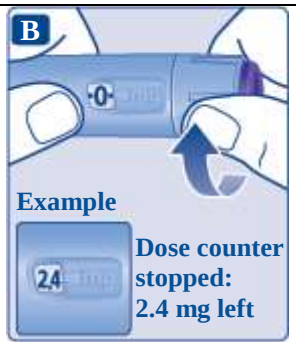
How much solution is left?

- The **pen scale** shows you **approximately** how much solution is left in your pen.

- **To see precisely how much solution is left,** use the dose counter:

Turn the dose selector until the **dose counter stops.**

If it shows 3,0, **at least 3,0 mg** are left in your pen. If the **dose counter stops before 3,0 mg,** there is not enough solution left for a full dose of 3,0 mg.



If you need more medicine than what is left in your pen

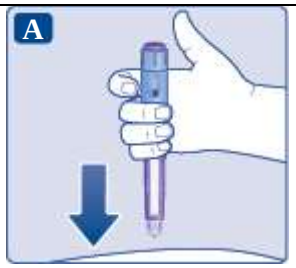
Only if trained or advised by your doctor or nurse, you may split your dose between your current pen and a new pen. Use a calculator to plan the doses as instructed by your doctor or nurse.

⚠ **Be very careful to calculate correctly.**

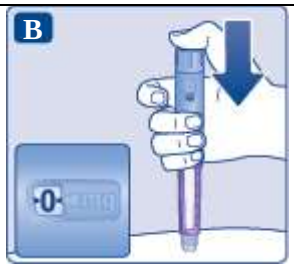
If you are not sure how to split your dose using two pens, then select and inject the dose you need with a new pen.

4. Inject your dose

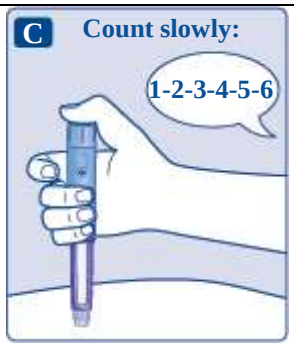
- **Insert the needle into your skin** as your doctor or nurse has shown you.
- **Make sure you can see the dose counter.** Do not cover it with your fingers. This could interrupt the injection.



- **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.

⚠ **Always watch the dose counter to know how many mg you inject**. Hold the dose button down until the dose counter shows 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.

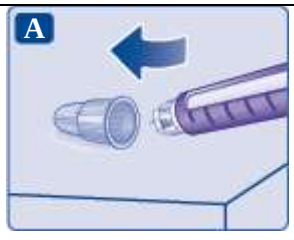
How to handle a blocked needle?

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.

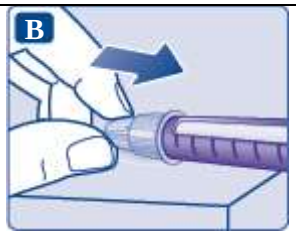
Never touch the dose counter when you inject. This can interrupt the injection.

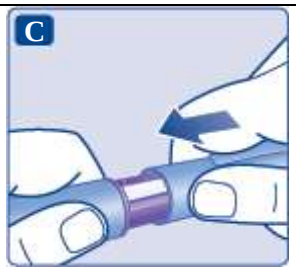
5. After your injection

- **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 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 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

- **Do not leave the pen in a car** or other place where it can get too hot or too cold.
- **Do not inject Saxenda® which has been frozen.** If you do that, you may 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.