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Summary of the risk management plan (RMP) for Saxenda (liraglutide)

This is a summary of the risk management plan (RMP) for Saxenda, which details the measures to be taken in order to ensure that Saxenda is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Saxenda, which can be found on Saxenda's EPAR page.

Overview of disease epidemiology

Saxenda is a medicine used along with diet and exercise to treat obesity, which is defined as a BMI (body-mass index, a measure of weight relative to height) of 30 or more; it can also be given to overweight patients (with BMI between 27 and 30) who have weight-related complications. Obesity can significantly reduce mental and physical health and quality of life, and can be associated with wide-ranging complications including high blood pressure, high blood sugar levels (diabetes), coronary heart disease, stroke, some types of cancer and sleep apnoea (frequent interruption of breathing during sleep).

About 25% of the world population was estimated to be overweight in 2005. Within Europe, it is anticipated that up to 2 out of 3 people will be obese or overweight within the next 10 years. The most prominent reason for obesity is excess calorie intake combined with reduced physical activity.

Summary of treatment benefits

Saxenda contains the active substance liraglutide, a 'glucagon-like peptide-1 (GLP-1) receptor agonist'. Liraglutide is already authorised in the EU as Victoza at lower doses (up to 1.8 mg per day) for the treatment of type 2 diabetes.

Saxenda has been shown to be effective at reducing body weight in 5 main studies involving over 5,800 obese or overweight patients, in which Saxenda was compared with placebo (a dummy treatment). Patients in the studies were given the medicine as part of a weight loss programme involving counselling and advice on diet and exercise.

Looking at the results of the 5 studies together, Saxenda at a daily dose of 3 mg led to a 7.5% reduction in weight, compared with a 2.3% reduction in patients taking placebo. Patients treated with Saxenda had a continuous decrease in weight during the first 40 weeks of treatment, after which the weight loss achieved was maintained. Weight loss was more pronounced in women than in men.

Unknowns relating to treatment benefits

Treatment benefits have not been established for the following groups of patients, and therefore use of Saxenda in these patients is not recommended:

- patients over 75 years of age and below 18 years of age;

- patients with liver problems;
- patients with severe kidney problems;
- patients treated with other medicines for weight management;
- patients with obesity due to eating or hormonal disorders or to treatment with other medicines that may cause weight gain.

The benefit of using Saxenda for a very long time is also not known.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Low blood sugar levels when used in combination with diabetes medicines	When patients with type 2 diabetes are treated with both Saxenda and a type of diabetes medicine called a sulphonylurea, there is an increased risk of developing low blood sugar levels. This is because Saxenda has also an effect in controlling blood sugar levels. The use of Saxenda in diabetic patients also taking insulin has not been evaluated.	When Saxenda is used with a sulphonylurea, the doctor may consider reducing the dose of the sulphonylurea to lower the risk of low blood sugar levels.
Side effects related to the stomach and gut (such as vomiting and diarrhoea)	Side effects such as nausea (feeling sick), diarrhoea, constipation, heartburn and vomiting are very common when taking Saxenda (they occur in more than 1 patient in 10). These reactions usually disappear after a few weeks of treatment.	To limit these effects, when starting treatment the dose of Saxenda should be slowly increased over 4 weeks.
Loss of fluids (dehydration) and kidney problems (altered renal function)	When starting treatment with Saxenda, the patient may feel sick (and may not eat and drink as much as usual), or may be sick or get diarrhoea (as mentioned above). This can lead to loss of fluids, which in turn may affect how well the kidneys work.	In case of vomiting, nausea and diarrhoea, it is important to drink plenty of fluids.
Allergic reactions	Few cases of allergic reactions have been reported with Saxenda. Symptoms include skin rash, low blood pressure, palpitations and difficulty breathing.	Saxenda should not be used in patients who are allergic to liraglutide or to any of the other ingredients of the medicine. If an allergic reaction is suspected treatment with Saxenda should be stopped and not restarted.
Gallstones and inflammation of the gallbladder	Gallstones have been reported in up to 1 patient in 10 taking Saxenda. Rapid weight loss increases the risk of developing gallstones. The risk is higher	Doctors should inform patients of the signs and symptoms of acute gallstone disease. In case of recurring attacks of severe stomach pain, it is important to

Risk	What is known	Preventability
	for women than men, and also increases with age.	consult a doctor.
Inflammation of the pancreas (pancreatitis)	Use of GLP-1 receptor agonists such as Saxenda has been associated with pancreatitis (inflammation of the pancreas, a small organ in the digestive system). Few cases of acute pancreatitis have been reported with Saxenda.	Doctors should inform patients of the signs and symptoms of acute pancreatitis. Patients who have a severe stomach ache which does not go away, should contact their doctor as this could be a sign of pancreatitis. If pancreatitis is suspected, Saxenda and other potentially suspected medicines should be discontinued. If acute pancreatitis is confirmed, Saxenda should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Important potential risks

Risk	What is known
Increase in blood sugar levels when used instead of insulin	Because liraglutide is also used as a diabetes medicine, there have been reports of patients who need insulin but were given liraglutide instead. This will result in blood sugar levels that are too high. As Saxenda does not contain insulin, it should not be used for the treatment of type 1 diabetes or for the treatment of a condition called ketoacidosis (high blood levels of ketones (acids)).
Cancers and tumours (neoplasms) including breast cancer, pancreatic cancer and medullary thyroid cancer	Obese patients have an increased risk of developing some types of cancer including breast cancer and pancreatic cancer. In rodents, the GLP-1 gut hormone has been shown to stimulate cell growth. The relevance of this finding in humans is unknown. When Saxenda was given to rats and mice for most of their lifetime, more medullary (C-cell) thyroid cancers were seen than usual. The relevance of these findings for humans is considered low. In addition, there have been concerns that medicines that work in the same way as liraglutide may increase the risk of cancer of the pancreas. When considering all the results from the use of Saxenda in humans, there are no conclusive data establishing a risk of cancers with Saxenda. Considering the seriousness of the conditions, cancers are considered an important potential risk.
Heart disease and stroke (cardiovascular disorders)	Obese patients have a higher risk of heart disease and stroke, which might lead to death. An increase in heartbeat has been seen in some patients treated with Saxenda during studies. On average, they had 2 to 3 more heart beats each minute. There are no conclusive data establishing a risk of heart disease or stroke with Saxenda. Considering the seriousness of these conditions, heart disease and stroke are considered important potential risks.
Lack of effect due to the body making	There is a concern that some patients make antibodies against Saxenda. This could potentially prevent Saxenda from functioning as intended. Antibodies

Risk	What is known
antibodies against Saxenda (lack of efficacy due to anti-liraglutide antibody formation)	have been detected in the blood of patients taking Saxenda. However, in clinical studies this has not been shown to reduce the effect of Saxenda.
The body's natural antibodies attach to a substance coming from outside the body (e.g., Saxenda) to form a compound called immune complex (immune complex disorders)	There is a theoretical risk that Saxenda could trigger the formation of an immune complex, which might get deposited in body organs and lead to organ failure. Although one case of immune complex disorders has been reported following the use of Saxenda, the origin was not clear and could have been related to other agents (e.g., microorganisms, other medicines). Immune complex disorders are considered an important potential risk since they are serious conditions.

Missing information

Risk	What is known
Use in children (below 18 years of age)	Saxenda has not been studied in patients under 18 years of age. This means that it is not known if Saxenda is safe and effective in this age group. Saxenda is not recommended for use in children.
Use in women who want to become pregnant, are pregnant or are breastfeeding	Saxenda has not been studied in pregnant women, women attempting to become pregnant or women who are breastfeeding. Saxenda should not be used during pregnancy since it is not known if Saxenda may harm the unborn child. Women should inform their doctor if they are planning to become pregnant or have become pregnant. Furthermore, it is not known if liraglutide, the active substance of Saxenda, passes into breast milk and therefore Saxenda should not be used when breastfeeding.
Use in patients with severely reduced liver function (severe hepatic impairment)	Saxenda has not been studied in patients with severely reduced liver function and use in these patients is not recommended. There is also not enough information about Saxenda used in patients with mild or moderately reduced liver function and Saxenda should be used with caution in these patients.
Use in patients with severely reduced kidney function (severe renal impairment)	Saxenda has not been studied in patients with severely reduced kidney function and use in these patients is not recommended. This includes patients with 'end-stage' kidney disease.
Use in patients with decreased ability of the heart to pump blood, leading to shortage of breath (congestive heart failure NYHA III–IV)	Saxenda has not been studied in patients with certain heart problems (moderate or severe congestive heart failure, when the heart cannot pump enough blood around the body). This means Saxenda cannot be recommended for use in these patients.

Risk	What is known
Use outside of its approved indications (off-label use)	Saxenda should only be used for weight management. Information on how well Saxenda works in other conditions or what side effects could be seen are not available.
Major depression	There is no information about Saxenda when used in patients with major depression. Therefore, use in these patients is not recommended.
Used with other weight-lowering medicines	There is no information about Saxenda when used in combination with other weight-lowering medicines. Therefore, the use of Saxenda in combination with other weight-lowering medicines is not recommended.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Saxenda can be found on Saxenda's EPAR page.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
EX2211-3748 LEADER	A long-term, multi-centre, international, randomised double-blind, placebo-controlled trial to determine liraglutide effects on cardiovascular events.	Cardiovascular disorders, neoplasms, pancreatic cancer, pancreatitis, anti-liraglutide antibody formation, congestive heart failure.	Ongoing	Final study report 30 Mar 2016
NN8022-1839 SCALE	Effect of liraglutide on body weight in non-diabetic obese subjects or overweight subjects with other conditions.	Neoplasms (including breast cancer)	Ongoing	Final report 27 Aug 2015
NN8022-1839 SCALE	Collect information on baseline breast cancer risk and potential confounders for all identified cases of breast cancer in study NN8022-1839	Neoplasms (including breast cancer)	Planned	27 Aug 2015

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
	(including prior history of breast cancer, family history of breast cancer, mutations in BRCA1/BRCA2 genes and age at menopause)			
EX2211-3748 LEADER	Collect information on baseline cancer risk and potential confounders for all identified cases of breast cancer in LEADER (including prior history of breast cancer, family history of breast cancer, BRCA1/BRCA2 status and age at menopause)	Neoplasms (including breast cancer)	Planned	30 Mar 2016
MTC registry MTC- 22341	A medullary thyroid cancer case series registry of at least 15 years duration to systematically monitor the annual incidence of medullary thyroid carcinoma in the US and to identify any increase related to the introduction of liraglutide into the marketplace.	Medullary thyroid cancer	Ongoing	Final report 15 Sep 2026
NN2211-3784, Optum Database study	Post-marketing safety surveillance to observe the safety profile of liraglutide when used in a real-life setting in the US. To describe and monitor the safety profile of liraglutide and compare the incidence of adverse events with other diabetes medicines commonly in use.	Neoplasms (including thyroid cancer, medullary thyroid cancer, pancreatic cancer and overall malignant neoplasms [including breast cancer]), serious hypoglycaemia, acute pancreatitis, acute renal failure, macrovascular conditions, microvascular conditions, thyroid events and	Ongoing	Final study report 31 Jan 2016

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
		hypersensitivity reactions		
NN2211-3880, CPRD study	To evaluate the safety of liraglutide in the UK population. To compare safety outcomes during current use of liraglutide with the safety outcomes during the use of other non-insulin diabetes medicines. **Addendum study in 3880:** A sub-study evaluating the potential risk of neoplasms in patients treated with liraglutide in combination with metformin and insulin	Neoplasms (including malignant neoplasms, pancreatic cancer and thyroid cancer, including medullary thyroid cancer), acute pancreatitis and macrovascular conditions	Ongoing	Final study report 30 Jun 2015
NN8022-4192	A mechanistic study to assess effects of liraglutide on gallbladder emptying and pancreatic enzymes.	Acute gallstone disease	Planned	Protocol submission: 3 months after approval in the EU
NN8022-4246	Drug utilisation study: Database study on the use of liraglutide in clinical practice using the Clinical Practice Research Datalink (CPRD, with questionnaires) in the UK.	Off-label use (Victoza used for treatment of weight management and Saxenda not used correctly according to approved label)	Planned	Protocol submission: 3 months after approval in the EU
NN8022-4241	Drug utilisation study: Retrospective chart review of medical records in Germany and Italy on the use of liraglutide in clinical practice.	Off-label use (Victoza used for treatment of weight management and Saxenda not used correctly according to approved label)	Planned	Protocol submission: 3 months after approval in the EU

Studies which are a condition of the marketing authorisation

None of the above studies are a condition of the marketing authorisation.

Summary of changes to the risk management plan over time

Major changes to the Risk Management Plan over time

Not applicable.

This summary was last updated in 03-2015.