Saxenda® - Solution for injection
Liraglutide 3 mg for Weight Management

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

Author
Regulatory Affairs
Novo Nordisk A/S
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1 Summary of the risk management plan (RMP) for Saxenda (liraglutide)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them. The RMP summary of Saxenda® is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the „Arzneimittelinformation“ approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Saxenda® in Switzerland is the „Arzneimittelinformation“ (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Novo Nordisk Pharma AG is fully responsible for the accuracy and correctness of the content of the here published summary RMP of Saxenda®.

2 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.

3 Summary of treatment benefits

Saxenda contains the active substance liraglutide, a ‘glucagon-like peptide-1 (GLP-1) receptor agonist’. Liraglutide is already authorised in Switzerland 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
Patients in the studies were given the medicine as part of a weight loss program 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.

4 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.
# 5 Summary of safety concerns

## 5.1 Important identified risks

<table>
<thead>
<tr>
<th>Risk</th>
<th>What is known</th>
<th>Preventability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low blood sugar levels when used in combination with diabetes medicines</td>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Side effects related to the stomach and gut (such as vomiting and diarrhoea)</td>
<td>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.</td>
<td>To limit these effects, when starting treatment the dose of Saxenda should be slowly increased over 4 weeks.</td>
</tr>
<tr>
<td>Loss of fluids (dehydration) and kidney problems (altered renal function)</td>
<td>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.</td>
<td>In case of vomiting, nausea and diarrhoea, it is important to drink plenty of fluids.</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>Few cases of allergic reactions have been reported with Saxenda. Symptoms include skin rash, low blood pressure, palpitations and difficulty breathing.</td>
<td>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.</td>
</tr>
<tr>
<td>Gallstones and inflammation of the gallbladder</td>
<td>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 for women than men, and also increases with age.</td>
<td>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 consult a doctor.</td>
</tr>
</tbody>
</table>

## 5.2 Important potential risks

<table>
<thead>
<tr>
<th>Risk</th>
<th>What is known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in blood sugar levels when used instead of insulin</td>
<td>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)).</td>
</tr>
</tbody>
</table>


Cancers and tumours (neoplasms) including skin cancer (melanoma), pancreatic cancer and a rare subtype of thyroid cancer which originates from the C-cells in the thyroid (medullary thyroid cancer [MTC])

Obese patients have an increased risk of developing some types of cancer, including 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 neoplasms with Saxenda®, including skin cancer, pancreatic cancer or MTC. Considering the seriousness of the conditions, neoplasms (including melanoma), pancreatic cancer and MTC are considered as important potential risks.

5.3 Missing information

<table>
<thead>
<tr>
<th>Risk</th>
<th>What is known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use in children (below 18 years of age)</td>
<td>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.</td>
</tr>
<tr>
<td>Use in women who want to become pregnant, are pregnant or are breastfeeding</td>
<td>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.</td>
</tr>
<tr>
<td>Use in patients with severely reduced liver function (severe hepatic impairment)</td>
<td>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.</td>
</tr>
<tr>
<td>Use in patients with severely reduced kidney function (severe renal impairment)</td>
<td>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.</td>
</tr>
<tr>
<td>Use in patients with decreased ability of the heart to pump blood, leading to shortage of breath (congestive heart failure NYHA IV)</td>
<td>Saxenda® has not been studied in patients with moderately/severely decreased pumping ability of the heart so called ‘moderate/severe heart failure’). Liraglutide in lower dose (Victoza®) has only been studied in subjects with moderate heart failure. No information related to use of liraglutide in severe heart failure is available. Therefore, Saxenda® is not recommended for use in patients with severe heart failure.</td>
</tr>
<tr>
<td>Use outside of its approved indications (off-label use)</td>
<td>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.</td>
</tr>
<tr>
<td>Major depression</td>
<td>There is no information about Saxenda when used in patients with major depression. Therefore, use in these patients is not recommended.</td>
</tr>
</tbody>
</table>
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.

6 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’.

This medicine has no additional risk minimisation measures.

7 Planned post-authorisation development plan

7.1 List of studies in post-authorisation development plan

Planned post-authorisation development plan

Table 6–14 List of studies in post-authorisation development plan

<table>
<thead>
<tr>
<th>Study/activity (including study number)</th>
<th>Objectives</th>
<th>Safety concerns /efficacy issue addressed</th>
<th>Status</th>
<th>Planned date for submission of (interim and) final results</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTC registry MTC- 22341</td>
<td>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.</td>
<td>Medullary thyroid cancer</td>
<td>Ongoing</td>
<td>Final report 15 Sep 2026</td>
</tr>
<tr>
<td>NN8022-4246</td>
<td>In market utilisation of liraglutide used for weight management in the UK: a study in the CPRD primary care database</td>
<td>Off-label use (Victoza® used for treatment of weight management and Saxenda® not used correctly according to approved label)</td>
<td>Planned</td>
<td>6-month progress report: June 2018 Final study report: December 2019</td>
</tr>
</tbody>
</table>
**NN8022-4241**  
In-market utilisation of liraglutide used for weight management in Europe: a retrospective medical record review study  
Off-label use (Victoza® used for treatment of weight management and Saxenda® not used correctly according to approved label)  
Planned  
6-month progress report: November 2017  
Final study report: November 2019

**NN8022-4192**  
To compare the effect of liraglutide 3.0 mg with placebo on postprandial gallbladder dynamics after 12 weeks of treatment in subjects with obesity and overweight  
Acute gallstone disease  
Started  
Submission of final study report: December 2017

Abbreviations: CPRD = Clinical Practice Research Datalink.

### 7.2 Studies which are a condition of the marketing authorisation

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

### 8 Summary of changes to the risk management plan over time

#### 8.1 Major changes to the Risk Management Plan over time

Not applicable.

This summary was last updated in 12-2018.