Victoza
(liraglutide)
solution for injection
6 mg/ml

Summary of the risk management plan (RMP) for

Victoza®

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1 Summary of the risk management plan (RMP) for *Victoza*® (liraglutide)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine but also in connection with larger changes such as extension of the indication. 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 *Victoza*® 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 / Information sur le médicament“ 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 *Victoza*® in Switzerland is the „Arzneimittelinformation /Information sur le médicament“ (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 Victoza®.

2 Overview of disease epidemiology

2.1 Epidemiology of the disease - Type 2 diabetes mellitus

Diabetes mellitus is a group of metabolic abnormalities characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. T2DM is a heterogeneous, chronic and progressive disease characterised by insulin resistance, along with relatively impaired beta-cell function.diabetes, being overweight, low physical activity and a diet high in calories are all known risk factors for developing the disease.

Cardiovascular disease (CVD), a common diabetes complication, is one of the leading causes of death among people with diabetes and can account for 50% or more of deaths due to diabetes in some populations.2 Smoking, obesity, diabetes, hypercholesterolaemia and hypertension are the main risk factors for CVD worldwide.

3 Summary of treatment benefits

What is the current standard of treatment?

For type 2 diabetes, there are usually several treatment choices to reduce the blood sugar.

1. The first step in the treatment of type 2 diabetes includes changes in lifestyle, such as having a healthy diet and exercising more.

2. Further treatment includes taking diabetes medicine (so called antidiabetic medication) in form of tablet(s) and/or injection(s). If one type of diabetes medicine is not enough (i.e., does not normalise the blood sugar), a second medicine is added.

3. Often, a combination of these medications may be needed to achieve an optimal blood sugar control.

Where does Victoza® fit in?

At present, there are 2 main types of antidiabetic medication that are injected. One is based on a hormone secreted in the pancreas, called insulin. The other is based on a hormone secreted in the gut, called glucagon-like peptide-1 (GLP-1). Victoza® belongs to the latter group. Victoza® is used by adults who have type 2 diabetes to control their blood sugar level. Victoza® helps the body reduce its blood sugar level only when the blood sugar is too high. Treatment with Victoza® can be added at any step of the treatment of type 2 diabetes.

Victoza® can be used in addition to standard of care treatment to reduce heart disease in adults who are at an increased risk for heart disease and have type 2 diabetes.

What studies have been done with Victoza®?

The effects of Victoza® were first tested in experimental models and animals before being studied in humans. Victoza® was investigated in 7 large studies involving more than 4,000 adults with type 2 diabetes.

Victoza® has been investigated in a large study involving more than 9,000 adults with type 2 diabetes who were at an increased risk of heart diseases.

What did the studies show?

The results from these studies showed that Victoza® is effective in lowering the blood sugar and keeping it down for a long time. Additionally, the results of the large study involving adults at an

increased risk of heart diseases showed that Victoza® is effective in reducing the risk of heart diseases and stroke in adults with type 2 diabetes.

4 Unknowns relating to treatment benefits

The following groups of patients have not been studied thoroughly in clinical trials, and the treatment benefits for these groups are therefore not fully documented:

- patients with liver problems
- patients with severe kidney problems requiring dialysis

Otherwise, all patient groups intended to be treated with Victoza® have been part of the studies.

5 Summary of safety concerns

5.1 Summary of safety concerns - Important potential risks

Risk	What is known	Preventability
Low blood sugar when used in combination with other anti-diabetes medications	Overall, few patients experience low blood sugar when taking Victoza®. However, when combining Victoza® with another antidiabetic medication, there is an increased risk of this happening.	When combining Victoza® with certain antidiabetic medications, it is important that the doctor evaluates if the patient needs to change the dose of the medication.
Side effects related to the stomach and gut (such as vomiting, diarrhoea)	Reactions such as nausea, diarrhoea, constipation, heartburn and vomiting are common when taking Victoza®. These reactions usually disappear after a few weeks of treatment.	Following the recommended dosing instruction reduces the severity of these reactions. It is therefore important to always use the medicine exactly as told by the doctor.
High blood sugar from stopping insulin	There have been reports where patients who are dependent on insulin have been given Victoza® instead. This will result in a too high blood sugar, which in turn can lead to coma and death.	As Victoza® is not an insulin, it should not be used for the treatment of type 1 diabetes or for the treatment of ketoacidosis.
Loss of fluids and kidney problems (altered renal function)	When starting the treatment with Victoza®, the patient may in some cases experience loss of fluids/dehydration. Because of that, the patient may feel nauseous (and not eat and drink as much as usual), be sick or get diarrhoea. This may lead to dehydration, which in turn may affect how well the kidneys work	In case of vomiting, nausea and diarrhoea, it is important to avoid dehydration by drinking plenty of fluids.
Allergic reactions	Victoza® can cause allergic reactions.	Victoza® should not be used if the patient is allergic to liraglutide or any of the other ingredients of the medicine.
Gallstones and inflammation of the gallbladder	Gallstones have been reported in up to 1 in 10 patients taking Victoza®.	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.

Abbreviations: GLP-1 = glucagon-like peptide-1

5.2 Summary of safety concerns – Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
A rare subtype of thyroid cancer which originates from the C-cells in the thyroid (Medullary thyroid cancer [C-cell carcinogenicity])	When Victoza® was given to rats and mice for most of their lifetime, more medullary (C-cell) thyroid cancers were seen. The relevance of these findings for humans is considered low. There are no conclusive data establishing a risk of MTC with liraglutide in humans. However, since it is a serious condition, MTC is considered a potential risk.

Abbreviations: MTC = medullary thyroid cancer; GLP-1 = glucagon-like peptide-1.

5.3 Summary of safety concerns - Missing information

Risk	What is known
Less than 18 years old (Use in children and adolescents)	Victoza® has only been studied in a few patients under 18 years. This means Victoza® cannot currently be recommended for use in this age group.
Women who want to become pregnant, are pregnant or are breastfeeding (Use in pregnant and lactating women)	Victoza® has not been studied in pregnant women, women attempting to become pregnant or women who are breastfeeding. Victoza® should not be used during pregnancy. It is not known if Victoza® may harm the unborn child. Furthermore, it is not known if Victoza® passes into breast milk. Victoza® should not be used when breastfeeding. The doctor should be informed if the patient is planning to become pregnant, there is suspicion of pregnancy or if the patient has become pregnant.
Decreased liver function (Use in patients with severe hepatic impairment)	There is not enough information about Victoza® used by patients with severe liver problems. However, investigations testing the effect of this medication in these patients have not raised any concerns or necessity to adjust the dose in patients with mild and moderate liver impairment. The use of Victoza® is not recommended in patients with severe liver disease.
Severe reduction of the kidney function in patients on dialysis (Use in patients with end-stage renal disease)	Victoza® has not been properly tested in patients with severe kidney problems on dialysis. There is not enough information about Victoza® used by patients with end-stage renal disease. This means Victoza® cannot currently be recommended for use in these patients.
Decreased ability of the heart to pump blood, leading to shortage of breath (Congestive heart failure NYHA IV)	Victoza® has not been studied in this group of patients. There is not enough information about Victoza® used by patients with severe heart failure. This means Victoza® cannot currently be recommended for use in these patients.
Use outside of what is recommended (Off-label use)	Victoza® might be used in situations other than those it is intended for. Victoza® should only be used for treatment of type 2 diabetes. Using Victoza® to treat other conditions might jeopardise the patients' safety.

The ability of a drug to decrease/increase the effect of warfarin. Warfarin reduces the ability of the blood to clot (Drug-drug interactions with warfarin)	Victoza® has not been properly tested in patients who also take medicines containing the substance warfarin. Patients taking such medications must inform their doctor so that necessary precautions can be taken.

Abbreviations: NYHA = New York Heart Association

6 Summary of additional 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, the risks and recommendations for minimising them. Information for patient is available in lay language in the package leaflet. The measures in these documents are known as routine risk minimisation measures.

There are no additional measures put in place to address safety concerns.

6.1 Planned post-authorisation development plan

Table 1 provides an overview of the post-authorisation development plan for Victoza®.

Table 1 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
	A medullary thyroid carcinoma 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

Abbreviations: CPRD = Clinical Practice Research Datalink; MTC = medullary thyroid cancer

Studies which are a condition of the marketing authorisation

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

6.2 Summary of changes to the risk management plan over time

Version	Date	Safety concerns	Comment
Edition 19 Version 1	07 Aug 2013	The RMP was updated in accordance with the new guidance on format of the risk management plan. Furthermore, terminology and wording have been aligned throughout the document to ensure consistency. The following risks were classified as not important and removed from the RMP: • Headache • Upper respiratory tract infection • Injection site reactions • Microvascular complications of the eye The following updates were made to the important risks: • **Hypoglycaemia** – changed to Hypoglycaemia in combination with other anti-glycaemic agents • **Neoplasm** – The potential risk of developing malignant neoplasms following treatment with combination insulin detemir + liraglutide + metformin is merged into the potential risk of neoplasms.	
Edition 19 Version 3	14 Jan 2014	• **Potential risk medullary thyroid cancer** was updated by adding **(c-cell)** was added to the name where missing. • **Immunogenicity** was added to immune complex disorders and anti-liraglutide antibody formation	

Version	Date	Safety concerns	Comment
		where missing	
Edition 19 Version 4	28 Jan 2014	• **Pancreatitis** was updated to an identified risk. • In the risk **Neoplasms,** frequencies and number of events for pancreatic cancer were added to the risk table. Pancreatic cancer was also reflected in the pharmacovigilance activities.	
Edition 20 Version 1	30 Apr 2014	• **Patients with moderate renal impairment** were removed from the missing information.	
Edition 20 Version 2	26 Jun 2014	**Pancreatic cancer** was added as a separate **important potential risk**	
Edition 20 Version 4	22 Aug 2014	**Overdose** was removed from the missing information.	
Edition 21 Version 1	27 Apr 2015	No change to the safety concerns.	The RMP was updated on the completion of the commitment: toxicology study in juvenile animals, NN212291.
Edition 22 Version 1	15 Jun 2015	No change to the safety concerns.	The RMP was updated due to the finalisation of the NN2211-3880 CPRD database study.
Version 26.0	22 Jun 2016	No change to the safety concerns.	The RMP was updated due to the finalisation of the NN2211-3874 Optum Research Database study
Version 27.0	20 Oct 2016	Based on the results of the LEADER trial, the following safety concerns were removed: • Identified risk: **Pancreatitis** • Potential risks: **cardiovascular disorders, immunogenicity: immune complex disorders,**	The RMP was updated due to the finalisation of the LEADER trial, a new indication was proposed for Victoza®.

Version	Date	Safety concerns	Comment
		immunogenicity: anti-liraglutide antibody formation, neoplasms' and **'pancreatic cancer'** • Missing information: **NYHA class III, Severe renal impaired patients, mild** and **moderate hepatic impairment.** The following was added: **Acute gallstone disease**' as an important identified risk	

This summary was last updated in June 2018.