EU Risk Management Plan for Liraglutide STADA & Ablymico 6 mg/ml solution for injection in pre-filled pen in type 2 diabetes mellitus & weight management (Liraglutide)

RMP version to be assessed as part of this application:

RMP Version number: 0.2

Data lock point for this RMP: 2026-Mar-11

Date of final sign off: 2026-Mar-11

Rationale for submitting an updated RMP: RMP was updated to implement indication extension of Ablymico in weight management.

Summary of significant changes in this RMP: Addition of indication ‘Children (6 to < 12 years)’ for Ablymico in weight management in Part I and VI; update of dosage information in Part I; update of referenced RMP in Part II: Module SVIII and Annex 7.

Other RMP versions under evaluation:

RMP Version number: Not applicable

Submitted on: Not applicable

Procedure number: Not applicable

Details of the currently approved RMP:

Version number: Not applicable

Approved with procedure: Not applicable

Date of approval (opinion date): Not applicable

QPPV Name: Dr. Andreas Iwanowitsch

QPPV Signature:

Table of content

Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance(s) **(INN or common name)**	Liraglutide
Pharmacotherapeutic group(s) (ATC Code)	Drugs used in diabetes, glucagon-like peptide-1 (GLP-1) analogues ATC code: A10BJ02
Marketing Authorisation Applicant	STADA Arzneimittel AG
Medicinal products to which this RMP refers	2
Invented name(s) in the European Economic Area (EEA)	Liraglutide STADA (in type 2 diabetes mellitus) Ablymico (in weight management)
Marketing authorisation procedure	Centralised
Brief description of the product	<u>Chemical class:</u> Liraglutide is an acylated human glucagon-like peptide-1 (GLP-1) analogue with 97 % amino acid sequence homology to endogenous human GLP-1. Liraglutide binds to and activates the GLP-1 receptor (GLP-1R).
	<u>Summary of mode of action:</u> **In type 2 diabetes mellitus** 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; binding to albumin; and higher enzymatic stability towards the dipeptidyl peptidase-4 (DPP-4) and neutral endopeptidase (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 cyclic adenosine monophosphate (cAMP). Liraglutide stimulates insulin secretion in a glucose- dependent manner. 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 minor delay in gastric emptying. Liraglutide reduces body weight and body fat mass through mechanisms involving reduced hunger and lowered energy intake, GLP-1 is a physiological regulator of appetite and food intake, but the exact mechanism of action is not entirely clear. **In weight management** GLP-1 is a physiological regulator of appetite and food intake, but the exact mechanism of action is not entirely clear. In animal studies, peripheral administration of liraglutide led to uptake in specific brain regions involved in regulation of appetite, where liraglutide, via specific activation of the GLP- 1R, increased key satiety and decreased key hunger signals, thereby leading to lower body weight.
	<u>Important information about its composition:</u> Not applicable
Hyperlink to the Product Information	The product information is included in Module 1.3.1 of the eCTD sequence.
Indication(s) in the EEA	Current: **In type 2 diabetes mellitus** Liraglutide STADA is indicated for the treatment of adults, adolescents and children aged 10 years and above 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 • in addition to other medicinal products for the treatment of diabetes. **In weight management** <u>Adults</u> Ablymico is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial Body Mass Index (BMI) of: • ≥ 30 kg/m² (obesity), or • ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (prediabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea. Treatment with Ablymico should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5 % of their initial body weight.

	Adolescents (≥ 12 years) Ablymico can be used as an adjunct to a healthy nutrition and increased physical activity for weight management in adolescent patients from the age of 12 years and above with: • obesity (BMI corresponding to ≥ 30 kg/m^2 for adults by international cut-off points) and • body weight above 60 kg. Treatment with Ablymico should be discontinued and re-evaluated if patients have not lost at least 4 % of their BMI or BMI z score after 12 weeks on the 3.0 mg/day or maximum tolerated dose. Children (6 to < 12 years) Ablymico is indicated as an adjunct to healthy nutrition and increased physical activity for weight management in children from the age of 6 to < 12 years with • obesity (BMI ≥ 95th percentile) and • body weight ≥ 45 kg Treatment with Ablymico should be discontinued and re-evaluated if patients have not lost at least 4 % of their BMI or BMI z score after 12 weeks on the 3.0 mg/day or maximum tolerated dose.
Dosage in the EEA	Current: **In type 2 diabetes mellitus** Posology To improve gastrointestinal tolerability, the starting dose is 0.6 mg liraglutide daily. After at least one week, the dose should be increased to 1.2 mg. Some patients are expected to benefit from an increase in dose from 1.2 mg to 1.8 mg and based on clinical response, after at least one week, the dose can be increased to 1.8 mg to further improve glycaemic control. Daily doses higher than 1.8 mg are not recommended. When Liraglutide STADA is added to a sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia. Combination therapy with sulfonylurea is only valid for adult patients. Self-monitoring of blood glucose is not needed in order to adjust the dose of Liraglutide STADA. Blood glucose self-monitoring is necessary to adjust the dose of sulfonylurea and insulin, particularly when Liraglutide STADA therapy is started and insulin is reduced. A stepwise approach to insulin dose reduction is recommended.

	Method of administration Liraglutide STADA is for subcutaneous use. Liraglutide STADA must not be administered intravenously or intramuscularly. Liraglutide STADA is administered once daily at any time, independent of meals, and can be injected in the abdomen, in the thigh or in the upper arm. The injection site and timing can be changed without dose adjustment. However, it is preferable that Liraglutide STADA is injected around the same time of the day, when the most convenient time of the day has been chosen. Injection sites should always be rotated in order to reduce the risk of injection site amyloid deposits. **In weight management** Posology Adults 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 gastrointestinal tolerability. 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. Adolescents (≥ 12 years) For adolescents from the age of 12 to below 18 years old a similar dose escalation schedule as for adults should be applied. The dose should be increased until 3.0 mg (maintenance dose) or maximum tolerated dose has been reached. Daily doses higher than 3.0 mg are not recommended. Children (6 to < 12 years) For children from the age of 6 to below 12 years old a similar dose escalation schedule as for adults should be applied. The dose should be increased until 3.0 mg (maintenance dose) or maximum tolerated dose has been reached. Daily doses higher than 3.0 mg are not recommended. Liraglutide in children should be initiated by a physician experienced in the management of obesity in children.*Missed doses* 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. *Patients with type 2 diabetes mellitus* Ablymico should not be used in combination with another GLP-1 receptor agonist. When initiating Ablymico, it should be considered to reduce the dose of concomitantly administered insulin or insulin secretagogues (such as sulfonylureas) to reduce the risk of

	hypoglycaemia. Blood glucose self-monitoring is necessary to adjust the dose of insulin or insulin-secretagogues. Method of administration Ablymico is for subcutaneous use only. It must not be administered intravenously or intramuscularly. Ablymico 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 Ablymico is injected around the same time of the day, when the most convenient time of the day has been chosen. Injection sites should always be rotated to reduce the risk of injection site amyloid deposits.
Pharmaceutical form(s) and strengths	Current: 1 ml of solution contains 6 mg of liraglutide. One pre-filled pen contains 18 mg liraglutide in 3 ml.
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SII - Non-clinical part of the safety specification

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SIII - Clinical trial exposure

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SIV - Populations not studied in clinical trials

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SV - Post-authorisation experience

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SVI - Additional EU requirements for the safety specification

Since this RMP concerns a generic product, this section is not applicable.

Part II: Module SVII - Identified and potential risks

Not applicable. This is a generic application. There are no new data generated on differences with the originator’s product.

Part II: Module SVIII - Summary of the safety concerns

The safety concerns are aligned with the safety specifications for Victoza® (type 2 diabetes mellitus) and Saxenda® (weight management) as published with the latest RMP version (Novo Nordisk, V34.1, 28 May 2025, available on Saxenda | European Medicines Agency (EMA) (europa.eu), last updated on 31 July 2025, last accessed on 11 March 2026).

Table SVIII.1: Summary of safety concerns – **Liraglutide in type 2 diabetes mellitus**

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• Neoplasms (including melanoma) • Medullary thyroid cancer (C-cell carcinogenicity) • Pancreatic cancer
Missing information	• None

Table SVIII.2: Summary of safety concerns – **Liraglutide in weight management**

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• Neoplasms (including melanoma) • Medullary thyroid cancer (C-cell carcinogenicity) • Pancreatic cancer
Missing information	• Patients with a history of major depression or other severe psychiatric disorders • Concomitant use of other weight lowering products

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

There are no routine pharmacovigilance activities beyond adverse reactions reporting and signal detection.

Specific adverse reaction follow-up questionnaires for safety concerns:

None

Other forms of routine pharmacovigilance activities for safety concerns:

None

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are planned.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

No post-authorisation efficacy studies have been imposed or are planned.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product.

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2. Additional Risk Minimisation Measures

Not applicable.

V.3. Summary of risk minimisation measures

Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for Liraglutide STADA 6 mg/ml solution for injection in pre-filled pen in type 2 diabetes mellitus (Liraglutide)

This is a summary of the risk management plan (RMP) for Liraglutide STADA. The RMP details important risks of Liraglutide STADA, how these risks can be minimised, and how more information will be obtained about Liraglutide STADA's risks and uncertainties (missing information).

Liraglutide STADA's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Liraglutide STADA should be used.

This summary of the RMP for Liraglutide STADA should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Liraglutide STADA's RMP.

I. The medicine and what it is used for

Liraglutide STADA is authorised for the treatment of adults, adolescents and children aged 10 years and above with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise (see SmPC for the full indication). It contains liraglutide as the active substance and it is injected subcutaneously.

Further information about the evaluation of Liraglutide STADA’s benefits can be found in Liraglutide STADA’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage <link to the EPAR summary landing page>.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Liraglutide STADA, together with measures to minimise such risks and the proposed studies for learning more about Liraglutide STADA's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of Liraglutide STADA are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Liraglutide STADA. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information in type 2 diabetes mellitus	
Important identified risks	• None
Important potential risks	• Neoplasms (including melanoma) • Medullary thyroid cancer (C-cell carcinogenicity) • Pancreatic cancer
Missing information	• None

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Liraglutide STADA.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Liraglutide STADA.

Summary of risk management plan for Ablymico 6 mg/ml solution for injection in pre-filled pen in weight management (Liraglutide)

This is a summary of the risk management plan (RMP) for Ablymico. The RMP details important risks of Ablymico, how these risks can be minimised, and how more information will be obtained about Ablymico's risks and uncertainties (missing information).

Ablymico's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ablymico should be used.

This summary of the RMP for Ablymico should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Ablymico's RMP.

I. The medicine and what it is used for

Ablymico is authorised as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients; and to a healthy nutrition and increased physical activity for weight management in adolescent patients from the age of 12 years and above as well as in children from the age of 6 to < 12 years (see SmPC for the full indication). It contains liraglutide as the active substance and it is injected subcutaneously.

Further information about the evaluation of Ablymico’s benefits can be found in Ablymico’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage <link to the EPAR summary landing page>.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Ablymico, together with measures to minimise such risks and the proposed studies for learning more about Ablymico's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Ablymico is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Ablymico are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Ablymico. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information in weight management	
Important identified risks	• None
Important potential risks	• Neoplasms (including melanoma) • Medullary thyroid cancer (C-cell carcinogenicity) • Pancreatic cancer
Missing information	• Patients with a history of major depression or other severe psychiatric disorders • Concomitant use of other weight lowering products

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Ablymico.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Ablymico.

Annex 4 – Specific adverse drug reaction follow-up forms

Not applicable.

Annex 6 – Details of proposed additional risk minimisation activities (if applicable)

Not applicable.