LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Aglira,
(liraglutide (synthetic))

SE/H/2730/001/DC

This module reflects the scientific discussion for the approval of Aglira. The procedure was finalised at 2026-05-12. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.

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TABLE OF CONTENTS

I. Introduction 3
II. Executive summary 3
II.1 About the product 3
II.2 General comments on the submitted dossier 6
II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles ... 7
III. Scientific OVERVIEW AND DISCUSSION 8
III.1 Quality aspects 8
III.2 Non-clinical aspects 8
III.3 Clinical aspects 9
IV. BENEFIT RISK ASSESSMENT 13
V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION 13
V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC 13
V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC 13
V.3 Summary of Product Characteristics (SmPC) 14
V.4 Package Leaflet (PL) 14
V.4.1 Package Leaflet 14
V.4.2 Assessment of User Testing 14
VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY 15

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Aglira, 6 mg/ml, Solution for injection in pre-filled pen.

The active substance is liraglutide (synthetic). A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Indication and posology

Adults

Liraglutide 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 liraglutide 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)

Liraglutide 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 liraglutide 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.

*IOTF BMI cut-off points for obesity by sex between 12–18 years (see table 1), in accordance with study design of the Trial 4180, see section 5.1.

Table 1 IOTF BMI cut-off points for obesity by sex between 12–18 years

Age (years)	**BMI corresponding to 30 kg/m^2 for adults by international cut-off points.**	
	Males	**Females**
12	26.02	26.67
12.5	26.43	27.24
13	26.84	27.76
13.5	27.25	28.20
14	27.63	28.57
14.5	27.98	28.87
15	28.30	29.11
15.5	28.60	29.29
16	28.88	29.43
16.5	29.14	29.56
17	29.41	29.69
17.5	29.70	29.84
18	30.00	30.00

Children (6 to <12 years)

Liraglutide 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 Liraglutide 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.

*CDC BMI cut-off points for obesity (≥95th percentile) by sex between 6 to <12 years (see table 2), in accordance with study design of the Trial 4392, see section 5.1.

Table 2 Cut-off points for BMI (Weight in kg/Height in m^2) for obesity (≥95th percentile) by sex for children from 6 and < 12 years of age

Age (Years)	Obesity BMI ≥ 95th percentile	
	Males	**Females**
6	18.41	18.84
6.5	18.76	19.23
7	19.15	19.68
7.5	19.59	20.17
8	20.07	20.70
8.5	20.57	21.25
9	21.09	21.82
9.5	21.62	22.40
10	22.15	22.98
10.5	22.69	23.57
11	23.21	24.14
11.5	23.73	24.71

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 gastro-intestinal tolerability (see table 3). 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 3 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**	

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 (see table 3). 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 (see table 3). 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.

Mode of action
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).

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 GLP1R, increased key satiety and decreased key hunger signals, thereby leading to lower body weight. 11 GLP-1 receptors are also expressed in specific locations in the heart, vasculature, immune system and kidneys. In mouse models of atherosclerosis, liraglutide prevented aortic plaque progression and reduced inflammation in the plaque. In addition, liraglutide had a beneficial effect on plasma lipids. Liraglutide did not reduce the plaque size of already established plaques.

Special aspects
The reference product, Saxenda, is a biological medicinal product with the active substance liraglutide derived from Saccharomyces cerevisiae, whereas Aglira is manufactured synthetically.

The drug product is a solution for subcutaneous injection in pre-filled pen, 6.0 mg/mL of the drug substance presented in a pre-filled, multi-dose pen-injector.

Pharmacological classification
The ATC Code is A10BJ02, Pharmacotherapeutic group: Drugs used in diabetes, glucagon-like peptide 1 (GLP-1) analogues

II.2 General comments on the submitted dossier

The application for Aglira, 6 mg/ml, solution for injection in pre-filled pen, is a Hybrid Art. 10(3) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and the following concerned member states (CMS):

SE/H/2730: BG*, HR + *clockstop addition of* AT, CZ, ES, HU, NL, PL, PT, SK

**BG were initially CMS in SE/H/2730/001/DC, but were withdrawn from the procedure at Day 160.*

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Saxenda, 6 mg/ml, solution for injection in pre-filled pen, authorised in EU since 2015, with Novo Nordisk A/S as marketing authorisation holder.

Potential similarity with orphan medicinal products

Having considered the arguments presented and with reference to Article 8 of Regulation (EC) No141/2000, Aglira is considered not similar (as defined in Article 3 of Commission Regulation (EC) No. 847/2000) to Imcivree® 10 mg/ml solution for injection.
Therefore, with reference to Article 8 of Regulation (EC) No. 141/2000, the existence of any market exclusivity for Imcivree® 10 mg/ml solution for injection (Setmelanotide) in the treatment of pro-opiomelanocortin (POMC) deficiency, leptin receptor (LEPR) deficiency, Bardet-Biedl syndrome (BBS), and acquired hypothalamic obesity (aHO) does not prevent the granting of the marketing authorisation of Aglira.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, 'close-out letters' or 'exchange of information' issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

GCP
A statement on the application of appropriate GCP standards in the submitted study has been provided. The Applicant provided outcomes from inspections conducted around the time the study was performed. No critical issues regarding GCP have been identified. No inspection of the submitted study is deemed necessary.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

Drug Product
The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
The application procedure refers to Article 10(3) hybrid application. In line with this type of procedure, applicant submitted a non-clinical overview based on bibliographical data. The applicant has also conducted two GLP in vivo studies (14-days repeat toxicology studies in rats and rabbits) aimed to demonstrate the safety of liraglutide 6 mg/mL solution for injection and included these studies in the overview

The non-clinical overview, dated December 2024 refers to 63 publications, the most recent from year 2024.

Pharmacodynamic, pharmacokinetic and toxicological properties of liraglutide are well known. As liraglutide is a widely used, well-known active substance, apart from the toxicology studies, the applicant has not provided additional studies.

Non-clinical sections of the SmPC are in accordance with the SmPC of the reference product

The following non-clinical in vivo studies were submitted:

- 14-day repeated dose subcutaneous toxicity study of liraglutide 6 mg/mL solution for injection in Sprague Dawley rats

- 14-day repeated dose subcutaneous toxicity study of liraglutide 6 mg/mL solution for injection in New Zealand white rabbits

In the provided in vivo studies (which are not a requirement in the EU; conducted to meet local legislation from Medicines Agency), liraglutide was well tolerated and showed effects on body weight and food consumption in both species which are expected to occur due to the pharmacological activity of liraglutide. In rabbits, moderate dose-related vacuolation of hepatocytes in the liver were noted with unclear relevance.

Environmental Risk Assessment (ERA)
Aglira is a generic product with an approved reference medicinal product Saxenda (Liraglutide 6 mg/mL solution for injection in pre-filled pen)

According to the applicant the provided environmental risk assessment (ERA) document for liraglutide that has been conducted in line with the 2024 CHMP ERA Guideline.

The provided log pow value of liraglutide is approx. 0.4 estimated at pH 7.9 for aqueous solution, taken from read-across data (reference to ECHA, 2024) and therefore the applicant consider that liraglutide is readily biodegradable and does not present a bioaccumulation risk and an assessment for PBT is not necessary.
The applicant does not present any calculations of the PECsw value. Based on studies with reference product Saxenda the applicant states that the PECsw value is below the threshold limit of 0.01.

Liraglutide is a human GLP -1 analogue modified by a substitution of lysine by arginine, which are natural amino acids, and an incorporation of a natural fatty acid (palmitic acid), and is therefore considered to be a natural peptide/substance in line with the reference product Saxenda (EMA/217044/2021). The applicant consider Aglira a non-natural substance/peptide (due its structural modifications to extend the biostability and prolong the half-life of the peptide) but is excreted in low amounts (< 10%). Therefore, the applicant consider that there is no need for further studies according to the ERA guideline and that Aglira is unlikely to pose a risk to the environment. This is agreed.

III.3 Clinical aspects

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one (1) bioequivalence study in the fed state, comparing Liraglutide with the reference product Saxenda.

Pharmacokinetic properties of the active substance
Absorption: Liraglutide has an absolute bioavailability of (approximately) 55% after subcutaneous administration. The maximal plasma concentration after subcutaneous administration of 0.6 mg, was 9.4 nmol/l (for mean body weight of approximately 73 kg) and occur at around 8-12 hours.

The liraglutide can be administered independently of food intake, and therefore there are no restrictions with respect to food in the SmPC of the originator.

Linearity: The pharmacokinetics of liraglutide is linear, with a proportional increase in exposure with dose.

Elimination: The elimination half-life is approximately 13 hours.

Bioequivalence Study

Methods
This was a single-dose, two-way crossover study conducted in 47 healthy volunteers, comparing Liraglutide, 6 mg/ml, solution for subcutaneous injection in pre-filled pen, with Saxenda, 6 mg/ml, solution for subcutaneous injection in pre-filled pen, under fed conditions. Blood samples for concentration analysis were collected pre-dose and post-dose. Plasma concentrations of liraglutide were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max}.
Results
The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, , range) for liraglutide,

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	$AUC_{0-\infty}$ ng*h/ml	t_{max} h
***Ratio (90% CI)**	**94.77 (85.30 - 105.30)**	**98.71 (88.73 -109.80)**	**95.14 (86.00 - 105.25)**	**-**

AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
C_{max} maximum plasma concentration

**calculated based on ln-transformed data*

For AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Discussion and overall conclusion
The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr) and ICH M13A Guideline on bioequivalence for immediate-release solid oral dosage forms (EMA/CHMP/ICH/953493/2022). The bioanalytical methods were adequately validated.

From a pharmacokinetic point of view, based on the submitted bioequivalence study, Liraglutide could be considered bioequivalent with Saxenda.

Pharmacodynamics, Clinical efficacy, Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted.

The clinical efficacy and clinical safety can be assumed to be similar to that of the reference product, provided that the bioequivalence and quality issues (see the list of questions in section V), are resolved.

Pharmacodynamics
No new data have been submitted. No data are required for an abridged application provided bioequivalence has been satisfactorily demonstrated.

Efficacy
An adequate literature review has been performed and is acknowledged to support efficacy.

Safety
An adequate literature review has been performed and is acknowledged to support safety.

The BE study generated safety data. In this study 14.9% of participants in the test product group (Aglira) reported 12 AEs and 15.2% of participants reported 9 AEs in the reference (Saxenda) group. Reported AEs were gastrointestinal events and headache, all known as very common AEs for liraglutide.

Immunogenicity
No immunogenicity studies have been submitted. As 'sameness' compared to the reference product is considered proven, immunogenicity studies in vivo are not required.

Usability
The drug product consists of pharmaceutical product and medical device. The medical device is a non-refillable pen injector (pre-filled pen). Two documents/studies supporting similarity (and usability) between the two pre-filled pens i.e., DDP-LIRA-0433-032 Saxenda and Liraglutide 6 mg/ml Alina 50 Pen Injector Use Comparison and DDR-LIRA-0433-033 – Saxenda EU and Liraglutide 6mg/ml Alina 50 container closure system and performance comparison have been submitted.

The first study evaluated Instructions for use, device design dimensions, force of use and performance (dose accuracy and dose dispensing force) and the second study was a comparison between the reference product, Saxenda®, and proposed generic Liraglutide 6mg/mL Alina 50 pen injector, addressing primary packaging components, subassemblies, dimensions, design, and performance parameters such as dose dispensing force and dose accuracy.

There are some minor differences noted between the two pens. However, these are not considered clinically relevant and no human usability study is deemed necessary.

Pharmacovigilance system
SE/H/2730/001/DC Proposed MAH Teva GmbH: RMS, CZ, HU, NL, PL, PT, SK
SE/H/2730/001/DC Proposed MAH ratiopharm Arzneimittel Vertriebs-GmbH: AT
SE/H/2730/001/DC Proposed MAH Teva Pharma EAD: BG
SE/H/2730/001/DC Proposed MAH Teva Pharma S.L.U.: ES
SE/H/2730/001/DC Proposed MAH Teva B. V.: HR
The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System, together with an annex listing all relevant subsidiaries (including *ratiopharm Arzneimittel Vertriebs-GmbH*). Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

Risk Management Plan
The MAH have submitted risk management plans in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Aglira.

Part II Safety specification
The proposed summary of safety concerns is aligned with those of the reference product Saxenda (version 34.1).

Table SVIII.1: 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
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plans, version 1.1 signed 16-Oct-2025 (SE/H/2730/001/DC) is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)
Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the hybrid product, Aglira, is found adequate. There are no objections to approval of Aglira, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Post approval commitments
N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**

  N/A

- **Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83/EC**

  N/A

- **Specific obligation to complete post-authorisation measures for the marketing authorisation under Exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC**

  N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Saxenda, EMEA/H/C/003780/0000 for the content. For Design/layou the applicant has proposed a bridging to a user test carried out on a previously accepted user-tested leaflet material. The proposed bridging regarding layout is considered acceptable.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-