COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Linagliptine Vivanta 5 mg film-coated tablets (linagliptin)

NL/H/6671/001/DC

Date: 16 June 2026

This report reflects the scientific discussion for the approval of Linagliptine Vivanta 5 mg film-coated tablets. The procedure was finalised on 4 November 2025 in Slovenia (SI/H/0332/001/DC). After a transfer on 29 April 2026, the current RMS is the Netherlands. As a result, the product name, procedure number and layout have been updated in this report. For information on other changes after the transfer date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Linagliptine Vivanta 5 mg film-coated tablets, from Vivanta Generics s.r.o.

The product is indicated in:
adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as:
monotherapy

- when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.

combination therapy

- in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control.

A comprehensive description of the indications and posology is given in the current SmPC.

This concerns an application for marketing authorisation for Linagliptine Vivanta 5 mg film-coated tablets according to Article 10(1) (generic application) of Directive 2001/83/EC (as amended).

The active substance is not considered a new active substance. The reference medicinal products (brand leaders) referred to as authorised not less than 8/10 years in EEA is Trajenta 5 mg film-coated tablets, authorised by Community since August 24th, 2011, by Boehringer Ingelheim International GmbH.

II. QUALITY ASPECTS

II.1 Introduction

Linagliptin Vivanta 5 mg film-coated tablets are light brown, round (approximately 8 mm in diameter), biconvex film-coated tablet debossed with ''L'' on one side and ''5'' on the other side.

Tablets are packed in oPA/Alu/PVC//Alu blisters or oPA/Alu/PVC//Alu perforated unit dose blisters.

II.2 Drug Substance

Linagliptin is not described in the current Ph. Eur. or in USP. One source of active substance is proposed and ASMF procedure is used.

Manufacturing process
The manufacturing process consists of several chemical steps and crystallization. Starting materials are found acceptable.

Quality control of drug substance
The control tests and specifications for drug substance are adequately drawn up. Drug substance specification from drug product manufacturer is provided. The specification parameters and limits are the same as set in specification from drug substance manufacturer.

The batch analytical results indicate that the final API is of consistent quality and meets the predefined criteria.

Stability of drug substance
Stability studies have been performed with the drug substance. No significant changes in any parameters were observed. The proposed retest period and storage conditions are acceptable.

II.3 Medicinal Product

Pharmaceutical development
The drug product Linagliptine Vivanta 5 mg film-coated tablets is available as light brown colored, round shaped, biconvex, film-coated tablets debossed ''L'' on one side and ''5'' on other side., packed in OPA/Alu/PVC-Alu blister placed in a cardboard box with leaflet.
The development of the product has adequately been performed and described.

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

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

Quality control of drug product
The control tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose. Batch analysis has been performed on 3 batches. The batch analysis results show that the finished products meet the specifications proposed.

Stability of drug product

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.

The conditions used in the stability studies are according to the ICH stability guidelines.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

The applicant has submitted an adequate ERA. There is an earlier environmental risk assessment for linagliptin, which was carried out as part of the approval process for the originator Trajenta (EMEA/H/C/002110/0000). The data on the environmental risk assessment are published in the corresponding EPAR. The ERA contained all the necessary Phase I and II studies and was considered sufficient.

According to the Environmental Risk Assessment of Medicinal Products for Human Use, EMEA/CHMP/SWP/4447/00 Rev. 1 no further risk assessment in case of this generic product is necessary.

III.2 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of linagliptin are well known. As linagliptin is a widely used and well-known active substance, the applicant has not provided additional non-clinical studies, and no further studies are required.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate.

The non-clinical sections of SmPC are in line with those of the originator.

IV. CLINICAL ASPECTS

IV.1 Introduction

To support the application, the applicant has submitted one pivotal bioequivalence study with the 5 mg strength.

The clinical overview on the clinical pharmacology, efficacy and safety is provided and it is appropriate. Safety and efficacy of the present formulation is based on the safety and efficacy of the previously approved reference product. The clinical overview on the clinical pharmacology, efficacy and safety of linagliptin is sufficient.

IV.2 Pharmacokinetics

It is confirmed that the test product used in the bioequivalence study has the same quantitative composition and is manufactured by the same process as the one submitted for authorization.

Bioequivalence study

The study design employed open open-label, balanced, randomized, two-treatment, two-sequence, two-period, crossover, truncated, single-dose, oral bioequivalence study in healthy, adult human (male) subjects under fasting conditions according to the requirements of the Guideline on the Investigation of Bioequivalence.

Analytical/statistical methods

Bioanalytical method (LC-MS/MS) for the determination of linagliptin in K_2EDTA human plasma has been pre-study and in-study validated. The bioanalytical method validation report with seven addenda and the bioanalytical report have been enclosed. Also, Method SOP, Bioanalytical Study Plan, and relevant bioanalytical SOPs have been enclosed. Quality assurance statement, GLP statement, Certificates of analysis of reference standards and internal standards used in validation and in study samples analysis have been provided. The bioanalytical method for quantification of linagliptin in study samples (including the extraction method) is considered appropriate.

Results

Pharmacokinetic parameters for linagliptin N=37 (non-transformed values; arithmetic mean ± SD, tmax median, range)

Treatment	AUC_{0-72} (h*ng/mL)	C_{max} (ng/ml)	t_{max} (h)
Test	186.5973 ± 43.54411	5.4866 ± 2.08132	2.50 (0.50 - 12.00)
Reference	189.0137 ± 39.82229	5.7315 ± 1.74029	3.00 (1.00- 6.00)
***,**Ratio (90% CI)**	98.40 (96.14 - 100.72)	94.01 (87.55 - 100.93)	/

**ln-transformed values*

*** Intra Subject CV (Cmax <20%, AUC0-72<6%), Power 100%*

Based on the pharmacokinetic parameters of linagliptin, the test and reference product 5 mg formulations are considered bioequivalent after single-dose administration under fasting conditions. For AUC0-t and Cmax the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence study, Linagliptine Vivanta is considered bioequivalent with reference product TRAJENTA (linagliptin) 5 mg film-coated tablets of Boehringer Ingelheim International GmbH.

IV.3 Risk Management Plan

The Applicant has submitted a risk management plan, 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 Linagliptin 5 mg film-coated tablets.

Summary table of safety concerns as approved in RMP

Important identified risks	• Pancreatitis
Important potential risks	• Pancreatic cancer
Missing information	• Pregnancy/Breast-feeding

The proposed list of safety concerns is aligned with that of the reference medicinal product Trajenta (RMP, Version 13.1) and is considered acceptable.

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

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

The submitted Risk Management Plan, version 0.2, signed 14.5.2025 is considered acceptable.

IV.4 Discussion on the clinical aspects

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the reference product is demonstrated, additional data is not necessary.

The proposed common renewal date is 5 years after approval of the procedure, which is considered acceptable.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

This application concerns a generic medicinal product referencing Trajenta (linagliptin) 5 mg film-coated tablets of Boehringer Ingelheim International GmbH. Bioequivalence with the reference medicinal product has been demonstrated. No clinically relevant differences in efficacy or safety are anticipated in the proposed indication. Overall, the benefit/risk is considered positive and the medicinal products concerned are approvable.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-