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Public Assessment Report

Scientific discussion

Linagliptina Dr. Reddys 5 mg film-coated tablets linagliptin

ES/H/0961/001/DC

Date of this report:	10/12/2025

This module reflects the scientific discussion for the approval of Linagliptina Dr. Reddys 5 mg film-coated tablets. The procedure was finalised at 16/11/2025. For information on changes after this date please refer to the module 'Update'.

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I INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Linagliptina Dr. Reddys 5 mg film-coated tablets.

The product is indicated for:
The treatment of 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; or treatment 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 SmPC.

The marketing authorisation has been granted pursuant to Article 10.1 of Directive 2001/83/EC.

II EXECUTIVE SUMMARY

II.1 Rationale for the product

II.2 About the product

The active substance is Linagliptin. Linagliptin is an orally available, inhibitor of the enzyme DPP-4 (dipeptidyl peptidase 4, EC 3.4.14.5) an enzyme which is involved in the inactivation of the incretin hormones GLP-1 and GIP (glucagon-like peptide-1, glucose-dependent insulinotropic polypeptide). These hormones are rapidly degraded by the enzyme DPP-4. Both incretin hormones are involved in the physiological regulation of glucose homeostasis. Incretins are secreted at a low basal level throughout the day and levels rise immediately after meal intake. GLP-1 and GIP increase insulin biosynthesis and secretion from pancreatic beta cells in the presence of normal and elevated blood glucose levels. Furthermore GLP-1 also reduces glucagon secretion from pancreatic alpha cells, resulting in a reduction in hepatic glucose output. Linagliptin binds very effectively to DPP-4 in a reversible manner and thus leads to a sustained increase and a prolongation of active incretin levels. Linagliptin glucose-dependently increases insulin secretion and lowers glucagon secretion thus resulting in an overall improvement in the glucose homeostasis. Linagliptin binds selectively to DPP-4 and exhibits a > 10.000 fold selectivity versus DPP-8 or DPP-9 activity *in vitro.*

ATC code: A10BH05

The therapeutic indication, dosing regimen, route of administration and pharmaceutical form of the Applicant's product are the same as for reference's product – Trajenta® 5 mg film-coated tablets: Sitagliptin 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, or; in combination therapy with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control.

Posology
Linagliptin Dr.Reddys is available as 5 mg film-coated tablets.

The dose of linagliptin is 5 mg once daily. When linagliptin is added to metformin, the dose of metformin should be maintained, and linagliptin administered concomitantly. When linagliptin is used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin, may be considered to reduce the risk of hypoglycaemia (see section 4.4)

Special populations

Renal impairment

For patients with renal impairment, no dose adjustment for linagliptin is required.

Hepatic impairment
Pharmacokinetic studies suggest that no dose adjustment is required for patients with hepatic impairment but clinical experience in such patients is lacking.

Elderly
No dose adjustment is necessary based on age.

Paediatric population
A clinical trial did not establish efficacy in paediatric patients 10 to 17 years of age (see section 4.8, 5.1 and 5.2). Therefore, treatment of children and adolescents with linagliptin is not recommended. Linagliptin has not been studied in paediatric patients under 10 years of age.

Method of administration
The tablets can be taken with or without a meal at any time of the day. If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.

II.3 General comments on the submitted dossier

This decentralised application for a Marketing Authorisation for Linagliptin Dr Reddys 5 mg film-coated tablets is made under Article 10(1), generic application of Directive 2001/83/EC, as amended.

European Reference Product (ERP)
The European Reference Product which is used in Spain (RMS) and in PL and IT as CMS *(currently withdrawn)* is: Trajenta 5 mg film-coated tablets, (Boehringer Ingelheim International GmbH) registered in Europe since 23/08/2011 (EMEA/H/C/002110).

Assessment of similarity with authorised orphan medicinal product(s) under market exclusivity
Potential similarity with orphan medicinal products
Not applicable. In addition to this, pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the applicant did not submit a critical report in *Module 1.7 Information relating to Orphan Market Exclusivity*, addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

Derogation(s) from market exclusivity
Not applicable.

II.4 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

Valid current GMP certificates for finished product manufacturer, controllers and releasers are provided.

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 compliance
The study was conducted in accordance with Good Clinical Practice (GCP) standards. Monitoring reports and certificates of audits carried out by the Quality Assurance Unit are presented. The sites have been previously inspected by EU regulatory authorities.

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Introduction
The product Linagliptin 5 mg film-coated tablets, from Reddy Holding GmbH, consists of film-coated tablets containing 5 mg of linagliptin.
The maximum daily dose is 5 mg of Linagliptin.
Linagliptin 5 mg film-coated tablets are packed in the following primary packaging materials: OPA/Alu/PVC-Alu Blister Pack.

Drug substance
The chemical-pharmaceutical documentation and Quality Overall Summary in relation to Linagliptin 5 mg film-coated tablets are of sufficient quality in view of the present European regulatory requirements.

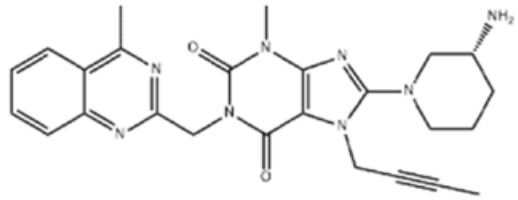
The ASMF procedure is used to support the quality of the drug substance.

General Information

Nomenclature:

INN: Linagliptin
Chemical name: 8-[(3R)-3-aminopiperidin-1-yl]-7-(but-2-yn-1-yl)-3-methyl-1-[(4-methylquinazolin-2-yl) methyl]-3, 7-dihydro-1H-purine-2,6-dione
CAS: 668270-12-0

Chemical structure:



Empirical Formula: $C_{25}H_{28}N_8O_2$
Molecular weight: 472.74

General Properties:

Appearance: Off-white to yellowish powder.
Solubility: Linagliptin is soluble in methanol, sparingly soluble in ethanol, slightly soluble in acetone, very slightly soluble in 2-propanol and practically insoluble in water.
Hygroscopicity: Slightly hygroscopic.
Stereochemistry and isomerism: The drug substance contains one chiral center.
Polymorphism: It exhibits polymorphism.
Melting range: 206.5 ºC.

Manufacture, process controls and characterisation

The description of the manufacturing process is properly detailed. The specifications of the materials used in the synthesis are sufficient and adequate. The profile of impurities, including residual solvents, of these materials which can influence the quality of the active substance are well defined and controlled. The acceptance criteria for the critical stages and the information on the quality and control of intermediates are adequate.

Specification, analytical procedures, batch analysis

Active substance specifications are considered appropriate and limits justified. Analytical methods are correctly described and validation carried out according to ICH. Batch results support consistent production.

Container closure system

The choice of the container closure system is properly justified. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. Protocol, controlled parameters and test methods are considered adequate. The packaging material is similar to that proposed for storage. Proposed re-test period and storage conditions are justified.

Drug Product

Description of the product

The description of the product is: White to off white, round, biconvex, bevel-edged, film coated tablets debossed with '5' on one side and plain on the other side. The approximate dimensions of finished product are 8.1 ± 0.2 mm (7.9 mm – 8.3 mm).

The qualitative composition of the finished product is as follows:

Tablet core

Linagliptin
Mannitol
Maize starch
Copovidone
Magnesium stearate

Film coating

Hypromellose
Macrogol
Talc

The packaging material intended for the commercial use consists in an OPA/Alu/PVC-Alu Blister Pack.

Pharmaceutical Development

The development of the product has been described, the choice of excipients is justified and their functions explained.
The physicochemical characteristics of the active substance that may affect the pharmaceutical form are identified and their control strategy is justified.

Manufacture of the product

The manufacturing process is fully described and in-process controls are appropriate considering the nature of the product and the manufacturing process. The industrial batch size is well-defined.
Sufficient validation data are provided.

Excipients

Excipients used are well known and of appropriate quality.
None of the excipients is of animal origin.

Product specification, analytical procedures, batch analysis

The finished product specifications are adequate to control the finished product. Provided description and validation data for the analytical methods are adequate. Batch analysis data have been submitted, and the results show that the finished product meets the proposed release specification.

Container closure system

The finished product is packaged in an OPA/Alu/PVC-Alu Blister Pack.

The choice of the container closure system is justified considering the nature of the finished product. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. The proposed protocol is considered adequate. The packaging material is the same as that intended for marketing. Proposed shelf-life and storage conditions are properly established.

Shelf-life: 30 months.

Storage conditions: This medicinal product does not require any special storage conditions.

III.2 Non clinical aspects

Critical evaluation of the Non-Clinical Overview and Summary

Pharmacodynamic, pharmacokinetic and toxicological properties of linagliptin are well known. As linagliptin is a widely used, well-known active substance, the applicant has not provided additional studies, and further studies are not required. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)

Since Linagliptina Dr. Reddys 5 mg film-coated tablets is a generic product, it will not lead to an increased exposure to the environment and therefore, additional ERA studies are not deemed necessary.

III.3 Clinical aspects

Linagliptin is an orally available, inhibitor of the enzyme DPP-4, a well-known active substance with established efficacy and safety. A clinical overview has been provided, which is based on scientific literature. The clinical overview justifies that there no need to generate additional clinical data.

For this generic application of an immediate release formulation, the MAH has submitted a bioequivalence study which is discussed below.

Pharmacokinetics

Biowaiver
N/A.

Bioequivalence studies
Study 0308-23

Clinical and analytical facilities
The clinical and analytical parts of the study were performed at Lambda Therapeutic Research Ltd., Lambda House, Plot No. 38, Survey No. 388, Near Silver Oak Club, S. G. Highway, Gota, Ahmedabad-382481, Gujarat, India.

Design
An open label, balanced, randomized, two treatment, two period, two sequence, single dose, crossover bioequivalence study was carried out in fasting conditions in 42 male subjects. The medication was administered as a single dose by oral route with 240 ± 2 mL of drinking water containing 20% glucose for reference and test film coated tablets in sitting posture. Subjects were refrained from drinking water from 1 hour before to 1 hour after dose administration except for 240 ± 2 mL of drinking water containing 20% glucose given with drug administration and 60 ± 1 mL of water containing 20% glucose at every 15 ± 5 minutes until 4 hours post-dose. There were two dosing periods, separated by a washout period of 42 days.

Analytical and statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples.
The 90% confidence interval (90% CI) of the ratio of the test formulation to the reference formulation for the log-transformed values of Cmax and AUC was calculated using an ANOVA model. This model included the covariates sequence, period, formulation and subject nested to sequence. Bioequivalence was defined when the 90% CI of the ratios (test/reference) for Cmax and AUC was in the range 80.00 -125.00%.
The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
42 subjects were included in the study. 42 subjects were treated; 37 subjects completed the study and 37 were used in the statistical analysis according to the protocol.
The inclusion and exclusion criteria are considered acceptable for a bioequivalence study.

Descriptive statistics

Pharmacokinetic Parameter	Arithmetic Means (± SD)	
	Test Product-T	Reference Product-R
$AUC_{(0-72)}$	216.652 ± 50.8340	210.572 ± 50.7489
C_{max}	5.428 ± 1.7083	5.430 ± 2.1888
t_{max}[1]	3.500 (0.750 - 24.000)	3.500 (0.750 - 12.000)

[1]Median (Min - Max).

Bioequivalence evaluation

Pharmacokinetic Parameter	Geometric Mean Ratio Test/Reference	90% Confidence Intervals	CV%[1]
$AUC_{(0-72)}$	103.1	100.29 - 106.04	7.1
C_{max}	101.8	95.39 - 108.63	16.6

Based on the statistical analysis submitted by the Applicant, the test product is equivalent to the reference with respect to the extent and rate of absorption/exposure as the 90% confidence intervals (90% CI) for the ln-transformed C_{max} and AUC_{0-72} are within the acceptance range of 80.00-125.00%.

Pharmacodynamics
NA

Clinical efficacy
NA

Clinical safety
NA

Summary Pharmacovigilance system

The Applicant has submitted a signed Summary of the Applicant's and/or Proposed Future MAH's* Pharmacovigilance System. P The PSMF provided does not comply 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 **satisfactory.**

* applicable in case the future MAH in RMS/CMSs will be different from the applicant

Risk Management Plan

The MAH has submitted a risk management plan (version 0.3, 27 August 2025), 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 Linagliptina Dr Reddys 5 mg film-coated tablets (linagliptin).

There are neither proposed additional pharmacovigilance activities nor proposed additional risk minimisation measures planned for Linagliptina Dr. Reddys 5 mg film-coated tablets.

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:

- 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.

Common renewal date
Five years after the finalization of the marketing authorisation procedure.

IV BENEFIT RISK ASSESSMENT

The quality of the generic product Linagliptina Dr. Reddys 5 mg film-coated tablets, is found adequate. There are no objections to the approval of Linagliptina Dr. Reddys 5 mg film-coated 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

In this section post approval commitments **not** falling under Article 21a or 22 should be included, e.g. as follows:

Description	Due date

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to 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 (PIL) has been performed based on a bridging report referring to Trajenta® authorised by centralised application. The bridging report submitted by the applicant has been found acceptable.

The results of the user consultation with target patient groups on the package leaflet submitted by the applicant show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

V.5 Labelling

The approved Labelling is available in the MRI Product Index.

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
-	-	-	-	-	-