Trajenta®
(linagliptin) 5mg tablets

# In 2021, Trajenta® marks 10 years since first regulatory approval. But, it took many more years to achieve that milestone.

**Start your journey and explore the key milestones for Trajenta® from discovery to registration .**


## 2000

Scientists at Boehringer Ingelheim first enter the search for novel **DPP4 inhibitors** for the treatment of type 2 diabetes.

## 2002

**Linagliptin (BI-1356) is discovered** as a promising DPP4i with a long duration of action, making it suitable for once daily dosing[1].



## 2004

After completion of the required non-clinical animal studies, linagliptin is tested in the **first Phase I clinical trial in human subjects**[2]. Ultimately, 24 Phase I trials would be included in the submission to regulatory authorities[3].

## 2006

After confirming a once-daily dosing regimen in Phase I, linagliptin advances to **Phase II testing in type 2 diabetes patients**[4]. In 4 Phase II trials, the efficacy and safety of linagliptin are assessed in relation to placebo and other antidiabetic drugs[3].



## 2008

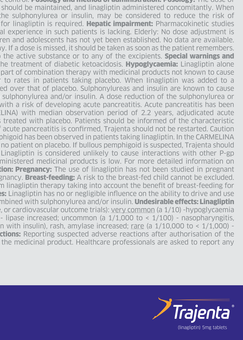
Linagliptin advances to **Phase III pivotal clinical trials**[5]. Data including 9 Phase III trials, in which nearly 4,000 T2D patients were treated with linagliptin, are eventually submitted to regulatory authorities[3].

## 2010

**New Drug Applications** are submitted to key regulatory agencies around the world for the approval of linagliptin.

The CAROLINA trial begins. This first cardiovascular outcome trial (CVOT) for Trajenta® ends up enrolling **more than 6,000 patients with relatively early T2D**. CAROLINA monitors the long-term CV safety profile of Trajenta® for a median of 6.3 years. With CAROLINA, linagliptin becomes the only DPP4i with a CVOT that includes an active comparator*.

CAROLINA®



## 2011



**Trajenta® becomes registered** in more than 30 countries around the world, as a once-daily, always one-dose, DPP4i for the treatment of type 2 diabetes[1]. In subsequent years, Trajenta® would become available in many more countries around the world.

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## 10 YEARS OF SIMPLICITY. 2021

**Happy 10 Year Anniversary Trajenta®**
In 2021, Trajenta® celebrates 10 years since its first regulatory approval.

### Footnotes

* CAROLINA included 6,033 patients with one or more of the following: a) previous vascular disease, b) evidence of vascular-related end-organ damage, c) age: ≥ 70 years and d) ≥ 2 CV risk factors (smoking, hypertension, T2D duration ≥ 10 years, dyslipidemia). CAROLINA assessed the CV safety profile of linagliptin vs. glimepiride.
† Trajenta® was approved by the US Food and Drug Administration (FDA) on May 2nd, 2011; Trazenta® was approved by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) on July 1st, 2011; Trajenta® was approved by the European Medicines Agency (EMA) on August 23rd, 2011; Trajenta® was approved by Health Canada on October 3rd, 2011; Trajenta® was approved by the Australian Therapeutic Goods Administration (TGA) on October 21st, 2011.

### Abbreviations

**CV**: cardiovascular; **CVOT**: cardiovascular outcome trial; **DPP4i**: dipeptidyl peptidase-4 inhibitor; **T2D**: type 2 diabetes.

### References


**1.** Eckhardt M, et al. J Med Chem 2007;50:6450-3. **2.** ClinicalTrials.gov, NCT02173665, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Rising Oral Doses of BI 1356 BS Administered to Healthy Male Subjects **3.** Trajenta® EMA Summary of Product Characteristics. October 2019. **4.** ClinicalTrials.gov, NCT00328172, Efficacy and Safety of 3 Doses of BI1356 (Linagliptin) in Type 2 Diabetes Patients. **5.** ClinicalTrials.gov, NCT00601250, Efficacy and Safety of BI 1356 (Linagliptin) vs. Placebo Added to Metformin Background Therapy in Patients With Type 2 Diabetes.


**Short version of the EU Summary of Product Characteristics (SPC) Medicinal Product: Trajenta® 5 mg film-coated tablets.**

Each tablet contains 5 mg of linagliptin. For the full list of excipients, consult section 6.1. of the full SPC.
**Therapeutic indications:** Trajenta is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as: a) monotherapy: when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment, b) combination therapy: in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control. **Posology and method of administration: Posology:** 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. **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:** The safety and efficacy of linagliptin in children and adolescents has not yet been established. No data are available. **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. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Special warnings and precautions for use:** Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. **Hypoglycaemia:** Linagliptin alone showed a comparable incidence of hypoglycaemia to placebo. In clinical trials of linagliptin as part of combination therapy with medicinal products not known to cause hypoglycaemia (metformin), rates of hypoglycaemia reported with linagliptin were similar to rates in patients taking placebo. When linagliptin was added to a sulphonylurea (on a background of metformin), the incidence of hypoglycaemia was increased over that of placebo. Sulphonylureas and insulin are known to cause hypoglycaemia. Therefore, caution is advised when linagliptin is used in combination with a sulphonylurea and/or insulin. A dose reduction of the sulphonylurea or insulin may be considered. **Acute pancreatitis:** Use of DPP-4 inhibitors has been associated with a risk of developing acute pancreatitis. Acute pancreatitis has been observed in patients taking linagliptin. In a cardiovascular and renal safety study (CARMELINA) with median observation period of 2.2 years, adjudicated acute pancreatitis was reported in 0.3% of patients treated with linagliptin and in 0.1% of patients treated with placebo. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Trajenta should be discontinued; if acute pancreatitis is confirmed, Trajenta should not be restarted. Caution should be exercised in patients with a history of pancreatitis. **Bullous pemphigoid:** Bullous pemphigoid has been observed in patients taking linagliptin. In the CARMELINA study, bullous pemphigoid was reported h 0.2% of patients on treatment with linagliptin and in no patient on placebo. If bullous pemphigoid is suspected, Trajenta should be discontinued. **Interaction with other medicinal products and other forms of interaction:** Linagliptin is considered unlikely to cause interactions with other P-gp substrates. Clinical data suggest that the risk for clinically meaningful interactions by co-administered medicinal products is low. For more detailed information on interactions with linagliptin, please consult the full version of the SPC. **Pregnancy and lactation: Pregnancy:** The use of linagliptin has not been studied in pregnant women. As a precautionary measure, it is preferable to avoid the use of linagliptin during pregnancy. **Breast-feeding:** A risk to the breast-fed child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from linagliptin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Effects on ability to drive and use machines:** Linagliptin has no or negligible influence on the ability to drive and use machines. However patients should be alerted to the risk of hypoglycaemia especially when combined with sulphonylurea and/or insulin. **Undesirable effects: Linagliptin 5 mg daily as monotherapy or as add-on therapy** (in clinical studies, post-marketing experience, or cardiovascular outcome trials): very common (≥ 1/10): hypoglycaemia (observed in combination with metformin plus sulphonylurea); common (≥ 1/100 to < 1/10) - lipase increased; uncommon (≥ 1/1,000 to < 1/100) - nasopharyngitis, hypersensitivity (e.g. bronchial hyperreactivity), cough, constipation (observed in combination with insulin), rash, amylase increased; rare (≥ 1/10,000 to < 1/1,000) - pancreatitis, angioedema, urticaria, bullous pemphigoid. **Reporting of suspected adverse reactions:** Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting systems.

**Revision date:** October 2019

Boehringer Ingelheim

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