

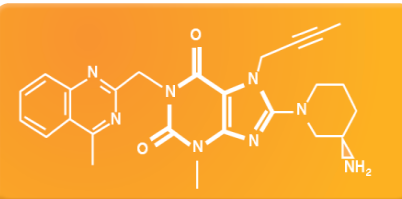
Linagliptin in Type 2 Diabetes

Media Fact Sheet

1. Linagliptin: A unique DPP-4 inhibitor
2. DPP-4 Inhibitors: A novel class of treatment in type 2 diabetes
3. Linagliptin: Phase III clinical trials programme

1. Linagliptin: A unique DPP-4 inhibitor

Linagliptin is the most advanced investigational compound for the treatment of type 2 diabetes within the Boehringer Ingelheim diabetes portfolio. Currently in late-stage phase III development, linagliptin belongs to the novel class of dipeptidyl peptidase (DPP)-4 inhibitors and is being developed as an oral, single-dose once-daily small tablet which can be taken time and food independent.



Overall, clinical studies to date have shown that linagliptin:¹⁻⁸

- can provide significant, sustained and clinically meaningful improvements in blood glucose control as monotherapy and in combination with other commonly used anti-diabetes drugs
- has an excellent safety and tolerability profile, no significant risk of hypoglycaemia and no clinically relevant interaction with most commonly used co-medications
- is weight neutral
- may not require dose adjustment in type 2 diabetes patients, regardless of the degree of renal impairment (linagliptin has a primarily non-renal route of excretion)

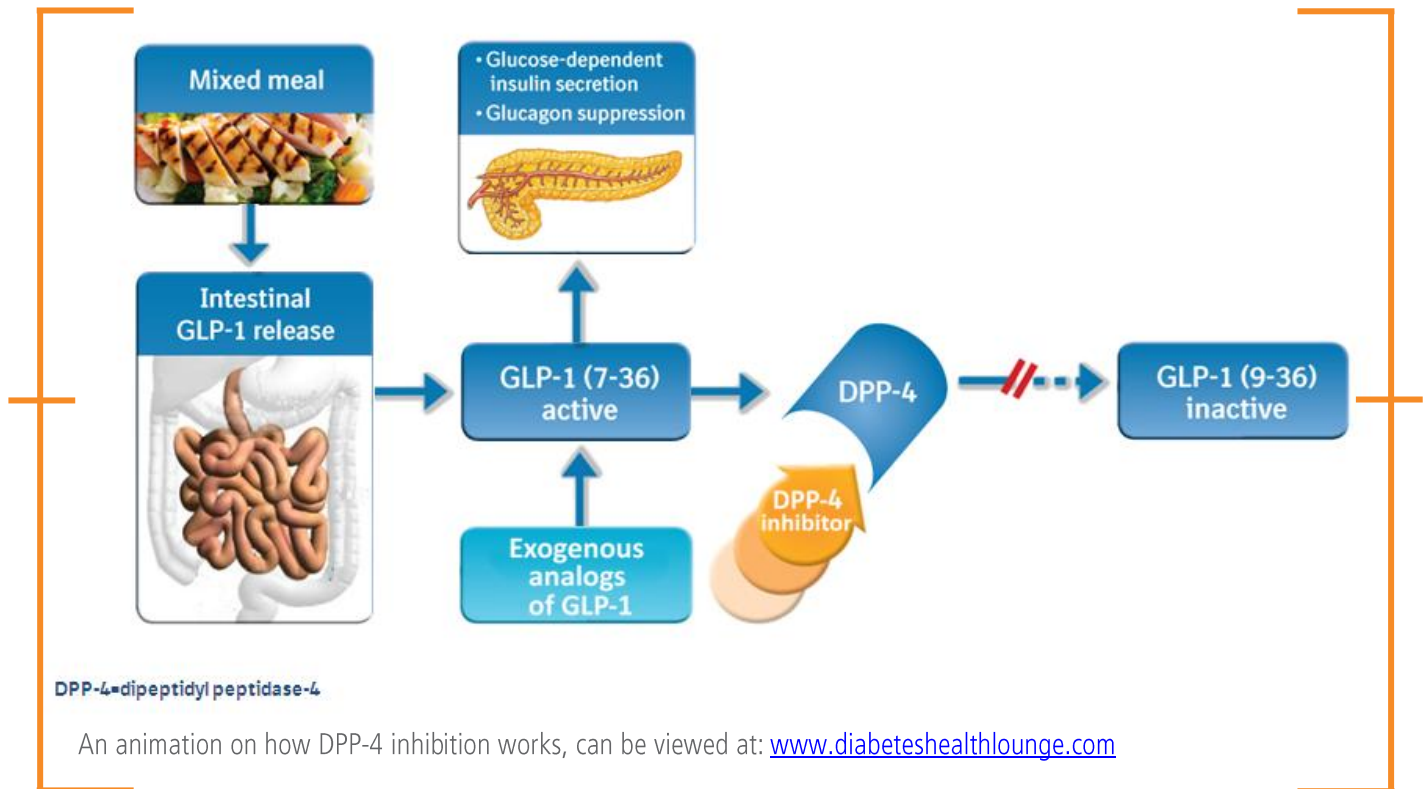
The phase III programme includes over 5,000 patients, with trial centres in over 40 countries across the globe.

2. DPP-4 Inhibitors: A novel class of treatment in type 2 diabetes

DPP-4 inhibitors represent an innovative approach to type 2 diabetes treatment with a unique mechanism of action compared to other classes in this therapeutic area.

By binding to the DPP-4 enzyme, they inhibit the breakdown of the two incretin hormones, glucagon-like peptide (GLP)-1 and glucose-dependent insulintropic peptide (GIP).⁹ GLP-1 and GIP are naturally occurring hormones, which are released by the gut after meals and target the pancreas by increasing glucose-dependent insulin secretion and suppressing glucagon secretion. DPP-4 inhibitors increase the GLP-1 plasma concentrations within the physiological range in contrast to injectable GLP-1 mimetics which have supra-physiological plasma levels and are associated with increased gastrointestinal side-effects, such as nausea and vomiting.^{9,10}

The mechanism of action of DPP-4 inhibitors^{11,12}



The inhibition of DPP-4 is beneficial for type 2 diabetes patients to control blood glucose levels, a primary goal of type 2 diabetes management.¹⁰ A dose-finding period (uptitration period) at the beginning of therapy is not needed when treating with a DPP-4 inhibitor.¹⁰ This is because of their rapid mode of action and the fact that their favourable tolerability profile does not cause nausea and vomiting,¹⁰ in addition to having a low risk of drug-drug interactions.¹³ This makes them appropriate as monotherapy or in combination with other commonly used anti-diabetes drugs.¹⁰

3. Linagliptin: Phase III clinical trials programme

Linagliptin: Clinical trials programme overview¹⁻⁸

The phase III clinical trials programme evaluates the safety, efficacy and tolerability of linagliptin alone and in combination with several commonly used diabetes treatments including metformin, sulphonylureas (SU) and thiazolidinediones (TZD). The overall linagliptin phase III clinical trials programme includes more than 5,000 patients, several hundred of them in different stages of renal impairment, as well as two independent longer term studies and investigations specifically into the safe and efficacious use of linagliptin in type 2 diabetes patients with mild, moderate and severe renal impairment.

Linagliptin: Results from linagliptin phase III clinical trials¹⁻⁸

EFFICACY

Overall, linagliptin was shown to provide significant, clinically meaningful and sustained improvements in glycaemic control as measured by changes in HbA_{1c} in monotherapy or in combination with most commonly used oral anti-diabetes drugs, such as metformin, sulphonylureas and thiazolidinediones.¹⁻⁸

Linagliptin has also shown that it may significantly improve parameters of β -cell function.^{3-6,8}

**SAFETY &
TOLERABILITY**

To date, linagliptin has shown an overall incidence of adverse events similar to placebo.¹⁻⁸ There was no significant increase in risk of hypoglycaemia attributed to linagliptin use in monotherapy or combination therapy with metformin, pioglitazone or sulphonylurea.¹⁻⁸ Linagliptin showed no clinically relevant interaction with most commonly used co-medications, suggesting that linagliptin could be given to all patients, regardless of any concomitant disease and with most commonly used co-medications.¹³⁻²⁰ Unlike treatments with sulphonylureas, thiazolidinediones or insulin, linagliptin is not associated with weight gain^{1-5,8,10,21} nor with the most common side effects associated with traditional anti-diabetes treatments.²¹ Contrary to many traditional treatments for type 2 diabetes,²² data to date suggest that linagliptin would not require a dose finding period (uptitration period) at the beginning of therapy.¹⁻⁸

CONVENIENCE

Linagliptin is the only oral anti-diabetes treatment that has a primarily non-renal route of excretion (only five percent of the oral administered dose is eliminated via the kidneys).²³ Studies have shown that linagliptin would be suitable for use in all patients with type 2 diabetes, even those with, or at risk of developing, renal impairment.^{5,6,20,24} Data to date support the assumption that no dose adjustment of linagliptin may be required in type 2 diabetes patients with any degree of renal impairment^{20,24} and, in contrast to many other anti-diabetes drugs, data suggest that linagliptin may not need additional monitoring of kidney function.²⁴

Related links:

More information about type 2 diabetes, associated complications and DPP-4 inhibitors can also be found at www.boehringer-ingelheim-webcast.com/diabetes, www.diabeteshealthlounge.com and www.youtube.com/diabetismatters.

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Please be advised: Linagliptin is an investigational drug and not yet approved for the treatment of type 2 diabetes. The information provided in this document is from Boehringer Ingelheim Corporate Headquarters in Germany. There may be national differences between countries regarding specific medical information included here. Please take account of this when referring to the information provided in this document. This document is for non-US healthcare media only.

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