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Prescribing information and adverse event reporting information is on the next page.

Trajenta®
(linagliptin) 5mg tablets

How to achieve treatment targets in adult type 2 diabetes and why is clinical inertia still an issue?

Why clinical inertia matters
Delayed treatment intensification due to clinical inertia may result in the development of irreversible diabetes-related complications[1]

In a retrospective cohort study, a 1-year delay in treatment intensification in people with uncontrolled type 2 diabetes significantly increased the risk of MI, HF, stroke and a composite endpoint of CV events[2]

The financial cost of clinical inertia

In the 2020–21 National Diabetes Audit, only 35.7% of people with type 2 diabetes in England and 28.2% of people with type 2 diabetes in Wales met all three treatment targets*[3]

Meeting all three treatment targets lowers the risk of diabetes-related complications and could save the NHS £727 million over 10 years[4]

40% of people with type 2 diabetes in the UK have an HbA1c level >53 mmol/mol (>7%)[5]

At a population level, the additional total UK economic burden for 7 years of poor glycaemic control is £2.6 billion[5]

*Having HbA1c ≤58 mmol/mol, blood pressure ≤140/80 mmHg and for people falling in the combined prevention CVD group, receiving statins[3]

Clinical inertia is multifactorial, with a range of contributing factors[6,7]

Patient-related factors
- Make up an estimated 30% of the causes of inertia
- Factors include concerns over side effects, misunderstanding of treatment regimens, multimorbidity and failure to reach target HbA1c

Physician-related factors
- Make up an estimated 50% of the causes of inertia
- Factors include time constraints, competing demands, lack of knowledge, variations in guideline recommendations and inexperience in type 2 diabetes management

Healthcare system-related factors
- Make up an estimated 20% of the causes of inertia
- Factors include healthcare issues and costs, and availability of medications and differences between healthcare settings

Examples of strategies for overcoming clinical inertia

Patient-related strategies[6]
- Use call–recall systems to remind patients about their appointments
- Encourage patients to access diabetes-specific education programmes
- Utilise technology (e.g. mobile apps) to aid diabetes self-management
- Provide psychological support to reduce fears and anxieties which may impact on treatment adherence

Physician-related strategies[6]
- Make use of the whole MDT, particularly in people with poorly controlled type 2 diabetes
- Access education to fill any existing knowledge gaps on type 2 diabetes
- Build the HCP–patient relationship and provide support to patients as needed for tight glycaemic control
- Use practice nurses and pharmacists for the management of type 2 diabetes and to free up GP time

Healthcare system-related strategies[6]
- Employ a multidisciplinary approach to improve the partnership between different specialties, increase confidence and build skills
- Integrate regular updates to other members of the MDT about patients' care into the service delivery plan
- Implement guidelines such as those individualised to overweight and obese patients into all healthcare systems to ensure appropriate intensification of therapy

In adults with type 2 diabetes, consider adding the DPP-4 inhibitor Trajenta (linagliptin):[8]

***As monotherapy when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment**

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

***When renal function is declining**

***In the frail/elderly person at risk of hypoglycaemia**

Remember:

One size may not fit all where HbA1c target setting is concerned[9]

Make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian[10]

CV: cardiovascular; DPP-4: dipeptidyl peptidase-4; GP: general practitioner; HF: heart failure; MDT: multidisciplinary team; MI: myocardial infarction

1. Khunti K, Millar-Jones D. Prim Care Diabetes 2017;11:3-12; 2. Paul SK et al. Cardiovasc Diabetol 2015;14:100; 3. NHS Digital (2022) National Diabetes Audit, 2020-21; Report 1: Care Processes and Treatment Targets. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit/core-report-1-2020-21 (accessed September 2023); 4. Diabetes UK (2019) Meeting type 2 treatment targets could save NHS millions. Available at: (accessed September 2023); 5. Bain S et al. J Med Econ 2020:23:98–105; 6. Khunti S et al. Ther Adv Endocrinol Metab 2019; 10: 1–11; 7. Okemah J et al. Adv Ther 2018; 5:1735–45; 8. TRAJENTA (linagliptin) Summary of Product Characteristics. Available at: www.medicines.org.uk (GB), www.emcmedicines.com/en-GB/northernireland/ (NI) and https://www.medicines.ie/medicines/trajenta-5-mg-film-coated-tablets-34014/spc (ROI) (accessed September 2023; 9. Strain WD et al. Diabetes Ther 2021;12:1227–47; 10. NICE (2022). Type 2 diabetes in adults: management. Available at: www.nice.org.uk/guidance/ng28 (accessed September 2023).

PC-GB-108416 | September2023

Prescribing Information (Great Britain) TRAJENTA® (Linagliptin)

Film-coated tablets containing 5 mg linagliptin. **Indication:** Trajenta 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. **Dose and Administration:** 5 mg once daily. If added to metformin, the dose of metformin should be maintained and linagliptin administered concomitantly. When 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:* no dose adjustment 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. 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 possible but a double dose should not be taken on the same day. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Warnings and Precautions: Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. *Hypoglycaemia:* 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:* Acute pancreatitis has been observed in patients taking linagliptin. 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. If bullous pemphigoid is suspected, Trajenta should be discontinued. **Interactions:** Linagliptin is a weak competitive and a weak to moderate mechanism-based inhibitor of CYP isozyme CYP3A4, but does not inhibit other CYP isozymes. It is not an inducer of CYP isozymes. Linagliptin is a P-glycoprotein substrate and inhibits P-glycoprotein mediated transport of digoxin with low potency. Based on these results and in *vivo* interaction studies, linagliptin is considered unlikely to cause interactions with other P-glycoprotein substrates. *Effects of other medicinal products on linagliptin:* The risk for clinically meaningful interactions by other medicinal products on linagliptin is low. Rifampicin: Multiple co-administration of 5 mg linagliptin with rifampicin, a potent inductor of P-glycoprotein and CYP3A4, decreased linagliptin steady state AUC and Cmax. Thus, full efficacy of linagliptin in combination with strong P-glycoprotein inducers might not be achieved, particularly if administered long term. Co-administration with other potent inducers of P-glycoprotein and CYP3A4, such as carbamazepine, phenobarbital and phenytoin has not been studied. *Effects of linagliptin on other medicinal products:* In clinical studies linagliptin had no clinically relevant effect on the pharmacokinetics of metformin, glibenclamide, simvastatin, warfarin, digoxin or oral contraceptives (please refer to Summary of Product Characteristics for a full list of interactions and clinical data). **Fertility, pregnancy and lactation:** The use of linagliptin has not been studied in pregnant women. As a precautionary measure, avoid use during pregnancy. 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. No studies on the effect on human fertility have been conducted for linagliptin. **Undesirable effects:** Adverse reactions reported in patients who received linagliptin 5 mg daily as monotherapy or as add-on therapies in clinical trials and from post-marketing experience. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) or very rare (<1/10,000). *Adverse reactions with linagliptin 5 mg daily as monotherapy:* Common: lipase increased. Uncommon: nasopharyngitis; hypersensitivity; cough; rash; amylase increased. Rare: pancreatitis; angioedema; urticaria; bullous pemphigoid. *Adverse reaction with linagliptin in combination with metformin plus sulphonylurea:* Very common: hypoglycaemia. Adverse reaction with linagliptin in combination with insulin: Uncommon: constipation. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 28 tablets £33.26. **Legal category**: POM. **MA number:** PLGB 14598/0225. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** September 2021.

PC-GB-100923 V23 Date of preparation July 2023

Prescribing Information (Northern Ireland) TRAJENTA® (Linagliptin)

Film-coated tablets containing 5 mg linagliptin. **Indication:** Trajenta 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. **Dose and Administration:** 5 mg once daily. If added to metformin, the dose of metformin should be maintained and linagliptin administered concomitantly. When 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:* no dose adjustment 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. Therefore, treatment of children and adolescents with linagliptin is not recommended. Linagliptin has not been studied in paediatric patients under 10 years of age. 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 possible but a double dose should not be taken on the same day. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. *Hypoglycaemia:* 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:* Acute pancreatitis has been observed in patients taking linagliptin. 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. If bullous pemphigoid is suspected, Trajenta should be discontinued. **Interactions:** Linagliptin is a weak competitive and a weak to moderate mechanism-based inhibitor of CYP isozyme CYP3A4, but does not inhibit other CYP isozymes. It is not an inducer of CYP isozymes. Linagliptin is a P-glycoprotein substrate and inhibits P-glycoprotein mediated transport of digoxin with low potency. Based on these results and in vivo interaction studies, linagliptin is considered unlikely to cause interactions with other P-glycoprotein substrates. *Effects of other medicinal products on linagliptin:* The risk for clinically meaningful interactions by other medicinal products on linagliptin is low. Rifampicin: Multiple co-administration of 5 mg linagliptin with rifampicin, a potent inductor of P-glycoprotein and CYP3A4, decreased linagliptin steady state AUC and Cmax. Thus, full efficacy of linagliptin in combination with strong P-glycoprotein inducers might not be achieved, particularly if administered long term. Co-administration with other potent inducers of P-glycoprotein and CYP3A4, such as carbamazepine, phenobarbital and phenytoin has not been studied. *Effects of linagliptin on other medicinal products:* In clinical studies linagliptin had no clinically relevant effect on the pharmacokinetics of metformin, glibenclamide, simvastatin, warfarin, digoxin or oral contraceptives (please refer to Summary of Product Characteristics for a full list of interactions and clinical data). **Fertility, pregnancy and lactation:** The use of linagliptin has not been studied in pregnant women. As a precautionary measure, avoid use during pregnancy. 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. No studies on the effect on human fertility have been conducted for linagliptin. **Undesirable effects:** Adverse reactions reported in patients who received linagliptin 5 mg daily as monotherapy or as add-on therapies in clinical trials and from post-marketing experience. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000) or very rare (<1/10,000). *Adverse reactions with linagliptin 5 mg daily as monotherapy:* Common: lipase increased. Uncommon: nasopharyngitis; hypersensitivity; cough; rash; amylase increased. Rare: pancreatitis; angioedema; urticaria; bullous pemphigoid. *Adverse reaction with linagliptin in combination with metformin plus sulphonylurea:* Very common: hypoglycaemia. *Adverse reaction with linagliptin in combination with insulin:* Uncommon: constipation. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 28 tablets £33.26. **Legal category:** POM. **MA number:** EU/1/11/707/003. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** May 2023.

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Prescribing Information (Ireland) TRAJENTA® (Linagliptin)

Film-coated tablets containing 5 mg linagliptin. **Indication:** Trajenta 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. **Dose and Administration:** 5 mg once daily. If added to metformin, the dose of metformin should be maintained and linagliptin administered concomitantly. When 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:* no dose adjustment 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. Therefore, treatment of children and adolescents with linagliptin is not recommended. Linagliptin has not been studied in paediatric patients under 10 years of age. 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 possible but a double dose should not be taken on the same day. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. *Hypoglycaemia:* 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: *Acute pancreatitis* has been observed in patients taking linagliptin. 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. If bullous pemphigoid is suspected, Trajenta should be discontinued. **Interactions:** Linagliptin is a weak competitive and a weak to moderate mechanism-based inhibitor of CYP isozyme CYP3A4, but does not inhibit other CYP isozymes. It is not an inducer of CYP isozymes. Linagliptin is a P-glycoprotein substrate and inhibits P-glycoprotein mediated transport of digoxin with low potency. Based on these results and in vivo interaction studies, linagliptin is considered unlikely to cause interactions with other P-glycoprotein substrates. *Effects of other medicinal products on linagliptin:* The risk for clinically meaningful interactions by other medicinal products on linagliptin is low. Rifampicin: Multiple co-administration of 5 mg linagliptin with rifampicin, a potent inductor of P-glycoprotein and CYP3A4, decreased linagliptin steady state AUC and Cmax. Thus, full efficacy of linagliptin in combination with strong P-glycoprotein inducers might not be achieved, particularly if administered long term. Co-administration with other potent inducers of P-glycoprotein and CYP3A4, such as carbamazepine, phenobarbital and phenytoin has not been studied. *Effects of linagliptin on other medicinal products:* In clinical studies linagliptin had no clinically relevant effect on the pharmacokinetics of metformin, glibenclamide, simvastatin, warfarin, digoxin or oral contraceptives (please refer to Summary of Product Characteristics for a full list of interactions and clinical data). **Fertility, pregnancy and lactation:** The use of linagliptin has not been studied in pregnant women. As a precautionary measure, avoid use during pregnancy. 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. No studies on the effect on human fertility have been conducted for linagliptin. **Undesirable effects:** Adverse reactions reported in patients who received linagliptin 5 mg daily as monotherapy or as add-on therapies in clinical trials and from post-marketing experience. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000) or very rare (<1/10,000). *Adverse reactions with linagliptin 5 mg daily as monotherapy:* Common: lipase increased. Uncommon: nasopharyngitis; hypersensitivity; cough; rash; amylase increased. Rare: pancreatitis; angioedema; urticaria; bullous pemphigoid. *Adverse reaction with linagliptin in combination with metformin plus sulphonylurea:* Very common: hypoglycaemia. *Adverse reaction with linagliptin in combination with insulin:* Uncommon: constipation. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes:** 28 tablets. **Legal category:** POM. **MA number:** EU/1/11/707/003. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. Additional information is available on request from Boehringer Ingelheim Ireland Ltd, 4045 Kingswood Road, Citywest Business Campus, D24 V06K. **Prepared in** May 2023

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Adverse events should be reported. Reporting forms and information can be found at https://www.mhra.gov.uk/yellowcard (UK) or https://www.hpra.ie/homepage/about-us/report-an-issue (IRE). Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone) (UK) or 01 2913960 (IRE), Fax: +44 1344 742661, or by e-mail: PV_local_UK_Ireland@boehringer-ingelheim.com.

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(linagliptin) 5mg tablets

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