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; however, clinical experience in patients ≥ 80 years of age is limited and caution should be exercised when treating this population. Paediatric population: the safety and efficacy of linagliptin in children and adolescents has not yet been established. No data are available. Take the tablets 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 ketoadidosis. 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: In post-marketing experience of linagliptin there have been spontaneously reported adverse reactions of acute pancreatitis. 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: 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 enzymes 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-gp substrates. The risk for clinically meaningful interactions by other medicinal products on linagliptin is low and in clinical studies linagliptin had no clinically relevant effect on the pharmacokinetics of metformin, gliperclamide, simvastatin, warfarin, digoxin or oral contraceptives (please refer to Summary of Product Characteristics for information on clinical data).

**Fertility, pregnancy and lactation:** 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 (frequencies identified from pooled analysis of placebo-controlled studies) in clinical trial and from post-marketing experience. The adverse reactions are listed by absolute frequency. 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), very rare (<1/10,000) or not known (cannot be estimated from the available data). Very common: hypoglycaemia (combination with/add-on to metformin and sulphonylurea); Common: lipase increased (monotherapy; combination with/add-on to metformin); pancreatitis (combination with/add-on to metformin and sulphonylurea);combination with/add-on to insulin, combination with/add-on to metformin and empagliflozin); Uncommon: nasopharyngitis (monotherapy; combination with/add-on to metformin); combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); cough (monotherapy; combination with/add-on to metformin; combination with/add-on to insulin; rash (monotherapy; combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin; amylose increased (combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); amylase increased (combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); rash (monotherapy; combination with/add-on to metformin; combination with/add-on to metformin and empagliflozin). Rare: angioedema (monotherapy; combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); urticaria (monotherapy; combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); cough (combination with/add-on to metformin and sulphonylurea; combination with/add-on to metformin and empagliflozin); pancreatitis (monotherapy; combination with/add-on to metformin; combination with/add-on to metformin and sulphonylurea; combination with/add-on to insulin); amylose increased (combination with/add-on to metformin; combination with/add-on to insulin). 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, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. Prepared in April 2017.
JARDIANCE® (empagliflozin) Prescribing information (UK)

Film-coated tablets containing 10 mg or 25 mg empagliflozin. **Indication:** Jardiance is indicated for the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise: as monotherapy when metformin is considered inappropriate due to intolerance; in addition to other medicinal products for the treatment of diabetes. For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, refer to the Summary of Product Characteristics.

**Dose and Administration:** The recommended dose is 10mg once daily. In patients tolerating empagliflozin 10mg once daily who have eGFR ≥ 60ml/min/1.73m² and need tighter glycaemic control, the dose can be increased to 25mg once daily. The maximum daily dose is 25mg. When concomitant use of a diuretic or insulin a lower dose of these may be recommended in patients 85 years or older. Very severe hepatic impairment: The glycaemic efficacy is dependent on renal function. No dose adjustment is required for patients with an eGFR ≥ 60ml/min/1.73m² or CrCl > 60ml/min. In patients tolerating empagliflozin whose eGFR falls persistently below 60ml/min/1.73m² or CrCl below 60ml/min, the dose of empagliflozin should be adjusted to or maintained at 10mg once daily. Discontinue when eGFR is persistently below 45ml/min/1.73m² or CrCl persistently below 45ml/min. Not for use in patients with end stage renal disease (ESRD) or on dialysis. Hepatic impairment: No dose adjustment is required in patients with hepatic impairment. Not recommended in severe hepatic impairment. Elderly patients: No dose adjustment is recommended based on age. In patients 75 years and older, an increased risk for volume depletion should be taken into account. Not recommended in patients 85 years or older.

**Paediatric population:** No data are available. **Method of administration:** The tablets can be taken with or without food, swallowed whole with water. 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. **Warnings and Precautions:** Not to be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis (DKA). Rare cases of DKA, including life-threatening and fatal cases, have been reported in patients treated with SGLT2 inhibitors, including empagliflozin. Consider the risk of DKA in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or weakness and assess patients for ketoacidosis immediately, regardless of blood glucose level. Interrupt treatment for patients hospitalised for major surgical procedures or acute serious medical illnesses. In patients where DKA is suspected or diagnosed, treatment should be discontinued immediately. Before initiating empagliflozin, consider factors in the patient history that may predispose to ketoacidosis. Use with caution in patients who may be at higher risk of DKA. **Renal impairment** and elderly: See under Dose and Administration; special attention should be given to volume intake of elderly patients in case of co-administered medicinal products which may lead to volume depletion (e.g. diuretics, ACE-inhibitors). Monitor renal function periodically and at least annually. Cases of hepatic injury have been reported with empagliflozin in clinical trials. A causal relationship between empagliflozin and hepatic injury has not been established. Haemocrit increase was observed with empagliflozin treatment. Osmotic diuresis accompanying therapeutic glucosuria may lead to a modest decrease in blood pressure. Therefore, caution should be exercised in patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years or older. In case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status and electrolytes is recommended. Temporary interruption of treatment with empagliflozin should be considered until the fluid loss is corrected. Temporary interruption of empagliflozin should be considered in patients with complicated urinary tract infections. An increase in cases of lower limb amputation (primarily of the toe) has been observed in ongoing long-term clinical studies with another SGLT2 inhibitor. Counsel patients on routine preventative footcare. Experience in New York Heart Association (NYHA) class I-II is limited, and there is no experience in clinical studies with empagliflozin in NYHA class III-IV. Due to its mechanism of action, patients taking Jardiance will test positive for glucose in their urine. The tablets contain lactose and should not be used in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption. **Interactions:** Use with diuretics may increase the risk of dehydration and hypotension. Insulin and insulin secretagogues may increase the risk of hypoglycaemia therefore, a lower dose of insulin or an insulin secretagogue may be required. The effect of UGT induction on empagliflozin has not been studied. Co-medication with known inducers of UGT enzymes should be avoided due to a potential risk of decreased efficacy. Interaction studies suggest that the pharmacokinetics of empagliflozin were not influenced by coadministration with metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, warfarin, verapamil, ramipril, simvastatin, torasemide and hydrochlorothiazide. Interaction studies conducted in healthy volunteers suggest that empagliflozin had no clinically relevant effect on the pharmacokinetics of metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, simvastatin, warfarin and other genetic infections and oral contraceptives. **Fertility, pregnancy and lactation:** There are no data from the use of empagliflozin in pregnant women. As a precautionary measure, it is preferable to avoid the use of Jardiance during pregnancy. No data in humans are available on excretion of empagliflozin into milk. Jardiance should not be used during breast-feeding. No studies on the effect on human fertility have been conducted for Jardiance. **Undesirable effects:** Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10,000 to <1/1000), not known (cannot be estimated from the available data). Very common: Hypoglycaemia (when used with sulphonylurea or insulin). Common: Vaginal moniliasis, vulvovaginitis, bacteraemias and other genital infections, urinary tract infection, thirst, pruritus (generalised), rash, increased urination, serum lipids increased. Uncommon: Urticaria, volume depletion, dysuria, blood creatinine increased/glomerular filtration rate decreased, haemocrit increased. Rare: DKA, Not known: Angioedema. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 10mg; 28 tablets £36.59, 25mg; 28 tablets £36.59. **Legal category:** POM. **MA numbers:** 10mg/28 tablets EU/1/14/930/013; 25mg/28 tablets EU/1/14/930/004. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany.


Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard

Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).
**Presentation** Abasaglar is a clear, colourless, sterile solution of 100 units/ml (equivalent to 3.64mg) insulin glargine (rDNA origin), available as either 3ml cartridge or 3ml KwikPen. Each cartridge/pen contains 300 units of insulin glargine in 3ml solution. **Uses** Treatment of diabetes mellitus in adults, adolescents, and children aged 2 years and above. **Dosage and Administration** The dose regimen (dose and timing) should be individually adjusted. In patients with Type 2 diabetes mellitus, Abasaglar can also be given together with orally active antidiabetic medication. Abasaglar has a prolonged duration of action, and should be administered once daily at any time, but at the same time each day. It should only be given by subcutaneous injection and should not be administered intravenously. Injection sites must be rotated within a given injection area from one injection to the next. Abasaglar must not be mixed with any other insulin or diluted. When switching from another intermediate or long-acting insulin treatment regimen to Abasaglar, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues, or the dose of oral antidiabetic medicinal products). To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Abasaglar should reduce their daily dose of basal insulin by 20-30 % during the first weeks of treatment. Abasaglar and Toujeo (insulin glargine 300 units/ml) are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycaemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily insulin glargine 300 units/ml to a once daily regimen with Abasaglar should reduce their dose by approximately 20%. During the first weeks the reduction should, at least partially, be compensated by an increase in mealtime insulin, after this period the regimen should be adjusted individually. Close metabolic monitoring is recommended during the switch and in the initial weeks thereafter. **Contra-indications** Hypersensitivity to insulin glargine or any of the excipients. **Warnings and Special Precautions** Abasaglar is not the insulin of choice for the treatment of diabetic ketoacidosis. In case of insufficient glucose control, or tendency to hyper- or hypoglycaemic episodes, other relevant factors must be reviewed before dose adjustment is considered. Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand, type, origin, and/or method of manufacture may result in the need for a change in dose. In rare cases, insulin antibodies may necessitate dose adjustment. The time of occurrence of hypoglycaemia may change when the insulin regimen is changed, depending on the action profile of the insulins used. Caution and intensified glucose monitoring are advised in patients for whom hypoglycaemia might be of particular clinical relevance. Patients should be aware that warning symptoms of hypoglycaemia may be changed, less pronounced, or absent in certain circumstances, including: markedly improved glycaemic control; when hypoglycaemia develops gradually; in the elderly; after transfer from animal to human insulin; autonomic neuropathy; long history of diabetes; psychiatric illness; use of certain medications such as beta-blockers. This may result in severe hypoglycaemia. The prolonged effect of insulin glargine may delay recovery from hypoglycaemia. If HbA1c is low, consider possibility of recurrent, unrecognised hypoglycaemia. Adherence of the patient to the dose and dietary regimen, correct insulin administration, and awareness of hypoglycaemia symptoms are essential to reduce risk of hypoglycaemia. Factors increasing risk of hypoglycaemia may require particularly close monitoring and may necessitate dose adjustment. Intercurrent illness requires intensified monitoring. Testing for ketones and dose adjustment may be necessary. Patients with Type 1 diabetes must continue to consume at least small amounts of carbohydrate and must never omit insulin entirely. The cartridges should only be used in a Lilly reusable insulin pen. The insulin label must always be checked before each injection to avoid medication errors. Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin. If the combination is used, patients should be observed for signs and symptoms of heart failure and pioglitazone discontinued if any deterioration occurs. **Fertility, Pregnancy and Lactation** No clinical data from controlled studies are available. Data from >1,000 pregnancy outcomes indicate no specific adverse effects of insulin glargine on pregnancy and no specific malformative nor feto/neonatal toxicity. The use of Abasaglar may be considered during pregnancy, if necessary. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly. Careful monitoring of glucose control is essential. **Effects on ability to drive and use machines** The patient’s ability to concentrate and react may be impaired as a result of hypo- or hyperglycaemia, or visual impairment. This may constitute a risk in situations where these abilities are of special importance (eg, driving a car or operating machines). **Undesirable Effects** Hypoglycaemia is very common. Injection site reactions and lipohypertrophy are common. Immediate-type allergic reactions are rare, but may be life-threatening. For full details of these and other side-effects, please see the Summary of Product Characteristics, which is available at http://www.medicines.org.uk/emc/. **Legal Category** POM **Marketing Authorisation Numbers** EU/1/14/944/003 EU/1/14/944/012 Cost £35.28 - 5 X 3ml cartridges £35.28 - 5 X 3ml KwikPens (80 Units) **Date of Preparation or Last Review** February 2017 **Full Prescribing Information is Available From** Eli Lilly and Company Limited Lilly House, Priestley Road Basingstoke, Hampshire, RG24 9NL Telephone: Basingstoke (01256) 315 000 E-mail: ukmedinfo@lilly.com Website: www.lillypro.co.uk ABASAGLAR® (insulin glargine) is a registered trademark of Eli Lilly and Company. KWIKPEN™ is a trademark of Eli Lilly and Company.