Film-coated tablets containing 2.5 mg linagliptin and 850 mg metformin hydrochloride or 2.5 mg linagliptin and 1,000 mg metformin hydrochloride.

**Indication:** Treatment of adult patients with type 2 diabetes mellitus: as an adjunct to diet and exercise to improve glycaemic control in adult patients inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of linagliptin and metformin; in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea; in combination with insulin (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in adult patients when insulin and metformin alone do not provide adequate glycaemic control. **Dose and Administration:** The dose should be individualised based on the patient's current regimen, effectiveness and tolerability, not exceeding the maximum recommended daily dose of 5 mg linagliptin plus 2,000 mg metformin hydrochloride. Patients inadequately controlled on maximal tolerated dose of metformin monotherapy; the usual starting dose should provide linagliptin 2.5 mg twice daily (5 mg total daily dose) plus the current metformin dose. Patients switching from co-administration of linagliptin and metformin: Initiate at the dose of linagliptin and metformin already being taken. Patients inadequately controlled on dual combination therapy or maximal tolerated dose of metformin and a sulphonylurea: The dose should provide linagliptin 2.5 mg twice daily (5 mg total daily dose) and a metformin dose similar to the dose already being taken. When linagliptin plus metformin hydrochloride is used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be required to reduce the risk of hypoglycaemia. Patients inadequately controlled on triple combination with insulin and the maximal tolerated dose of metformin: The dose should provide linagliptin 2.5 mg twice daily (5 mg total daily dose) and a metformin dose similar to the dose already being taken. When linagliptin plus metformin hydrochloride is used in combination with insulin, a lower dose of insulin may be required to reduce the risk of hypoglycaemia. Elderly: As metformin is excreted by the kidney, use with caution as age increases. Monitoring of renal function is necessary. Exercise caution in patients 80 years and older as clinical experience in this age group is limited. Renal impairment: Jentadueto must not be used in patients with moderate or severe renal impairment (creatinine clearance < 60 ml/min). Hepatic impairment: Not recommended. Clinical experience in patients with hepatic impairment is lacking. Paediatric population: Safety and efficacy in children and adolescents (aged 0 to 18 years) have not been established. No data are available. Taking Jentadueto: To be taken twice daily with meals. All patients should continue their diet with an adequate distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet. If a dose is missed, it should be taken as soon as the patient remembers. However, a double dose should not be taken at the same time (the missed dose should be skipped). Contraindications: Hypersensitivity to the active substances or to any of the excipients; diabetic ketoacidosis, diabetic pre-coma; renal failure or renal dysfunction (creatinine clearance < 60 ml/min); acute conditions with the potential to alter renal function such as dehydration, severe infection, shock; disease which may cause tissue hypoxia (especially acute disease, or worsening of chronic disease) such as decompensated heart failure, respiratory failure, recent myocardial infarction, shock; hepatic impairment, acute alcohol intoxication, alcoholism. Warnings and Precautions: Not to be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Caution is advised when Jentadueto is used in combination with a sulphonylurea and/or insulin due to increased incidence of hypoglycaemia. Lactic acidosis can occur due to metformin accumulation. If diagnosed the patient should be hospitalised immediately. Treatment should be temporarily discontinued in situations where renal function may become impaired e.g. dehydration (severe diarrhoea or vomiting), initiation of antihypertensive therapy, diuretic therapy or therapy with a non-steroidal anti-inflammatory drug (NSAID). Risk of lactic acidosis must also be considered, and treatment temporarily discontinued in patients with signs or symptoms of severe or non-specific muscle pain or tenderness, severe or persistent diarrhoea or vomiting, or other signs and symptoms suggestive of hypermetabolic and/or hypercatabolic conditions such as abdominal pain and severe asthenia. Patients should be alerted to the risk and symptoms of lactic acidosis. Serum creatinine levels should be determined before initiating treatment and regularly thereafter. Decreased renal function in older subjects is frequent and symptomatic. Special caution should be exercised in patients with renal function may become impaired. Renal function should be checked before initiating treatment with metformin. Patients with heart failure are more at risk of hypoxia and renal impairment. In patients with stable chronic heart failure Jentadueto may be used with regular monitoring of cardiac and renal function. Treatment must be discontinued 48 hours before elective surgery with general, spinal or epidural anaesthesia, or prior to, or at the time of intravascular administration of iodinated contrast agents in radiologic studies. Therapy should usually not be resumed earlier than 48 hours following surgery or must be not reintroduced until at least 48 hours after the test and only after renal function has been re-evaluated and found to be normal (surgery) or has not deteriorated further (radiologic studies). A patient with previously well controlled type 2 diabetes on Jentadueto who develops laboratory abnormalities or clinical illness (especially vague and poorly defined illness) should be evaluated promptly for evidence of ketoacidosis or lactic acidosis. If acidosis of either form occurs, stop treatment immediately and initiate other appropriate corrective measures. There have been spontaneously reported adverse reactions of acute pancreatitis with linagliptin. If pancreatitis is suspected, Jentadueto should be discontinued; if confirmed, treatment should not be restarted. Patients should be informed of the characteristic symptoms of acute pancreatitis. Exercise caution in patients with a history of pancreatitis. Interactions: Combination requiring precautions for use: glucocorticoids (given by systemic and local routes), beta-2-agonists, and diuretics. More frequent blood glucose monitoring should be performed, especially at the beginning of treatment with such medicinal products. If necessary, adjust the dose of Jentadueto during therapy with the other medicinal product and on its discontinuation. Adverse reactions known to occur with each active substance given singly but which have not been seen in clinical trials with Jentadueto, may occur during treatment with this medicinal product. If acidosis of either form occurs, stop treatment immediately and initiate other appropriate corrective measures. There have been spontaneous reports of acute lactic acidosis in acute alcohol intoxication. Cationic substances that are eliminated by renal tubular secretion e.g. cimetidine. The intravenous administration of iodinated contrast agents in radiologic studies may lead to renal failure, resulting in metformin accumulation and a risk of lactic acidosis (see above). Fertility, pregnancy and lactation: Jentadueto should not be used during pregnancy. If the patient plans to become pregnant, or if pregnancy occurs, discontinue treatment and switch to insulin treatment as soon as possible in order to lower the risk of foetal malformations associated with abnormal blood glucose levels. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Jentadueto 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 Jentadueto. Undesirable effects: 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 (≥ 1/100,000) and not known (cannot be estimated from the available data). Adverse reactions reported with the fixed dose combination: Uncommon: nasopharyngitis; cough; decreased appetite; diarrhoea; nausea; vomiting; rash; pruritus; blood amylase increased. Rare: hypersensitivity e.g. bronchial hyperreactivity; angioedema; urticaria. Not known: pancreatitis. Adverse reactions known to occur with each active substance given singly but which have not been seen in clinical trials with Jentadueto, may occur during treatment with this medicinal product. Additional adverse reactions reported when linagliptin and metformin were combined with insulin; common: liver function disorders. Uncommon: constipation. Additional information on individual components: Adverse reactions previously reported with one of the individual active substances may be potential adverse reactions with Jentadueto, even if not observed in clinical trials. Linagliptin: All identified adverse reactions of linagliptin monotherapy are also described for Jentadueto. Metformin: Known adverse reactions that were not reported in patients who received Jentadueto. Very common: abdominal pain. Common: taste disturbance. Very rare: lactic acidosis; vitamin B12 deficiency; hepatitis; skin reactions. Prescribers should consult the Summary of Product Characteristics for further information on side effects. Pack sizes and NHS price: 2.5 mg/850 mg 56 tablets £33.26; 2.5 mg/1,000 mg 56 tablets £33.26. Legal category: POM. MA numbers: 2.5 mg/850 mg (56 tablets) EU/1/12/780/505; 2.5 mg/1,000 mg (56 tablets) EU/1/12/780/109. 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 December 2015.