For the use only of Registered Medical Practitioner or a Hospital or a Laboratory

TRAJENTA DUO®

Composition: 1 film-coated tablet contains linagliptin 2.5 mg and metformin hydrochloride 500 mg, 850 mg or 1000 mg. **Indication**: TRAJENTA DUO® tablets are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both linagliptin and metformin is appropriate. It should not be used in patients with type 1 diabetes, or for the treatment of diabetic ketoacidosis. It has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using TRAJENTA DUO®. **Dosage and administration:** The dosage should be individualized based on both effectiveness and tolerability, while not exceeding the maximum recommended dose of 2.5 mg linagliptin/1000 mg metformin hydrochloride twice daily. It should be given twice daily with meals. Dose escalation should be gradual to reduce the gastrointestinal (GI) side effects associated with metformin use. Recommended starting dose: In patients currently not treated with metformin, initiate treatment with 2.5 mg linagliptin/500 mg metformin hydrochloride twice daily. In patients already treated with metformin, start with 2.5 mg linagliptin and the current dose of metformin taken at each of the two daily meals (e.g., a patient on metformin 1000 mg twice daily would be started on 2.5 mg linagliptin/1000 mg metformin hydrochloride twice daily with meals). Patients already treated with linagliptin, and metformin individual components may be switched to TRAJENTA DUO® containing the same doses of each component. When TRAJENTA DUO® is used in combination with an insulin secretagogue (e.g., sulfonylurea) or with insulin, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia. Pediatric Use: Safety and effectiveness of TRAJENTA DUO® in pediatric patients under 18 years of age have not been established. **Geriatric Use:** Linagliptin is minimally excreted by the kidney; however, metformin is substantially excreted by the kidney. Considering that aging can be associated with reduced renal function, TRAJENTA DUO® should be used with caution as age increases. **Pregnancy and Lactation:** The limited data with TRAJENTA DUO® and linagliptin use in pregnant women are not sufficient to inform a TRAJENTA DUO® -associated or linagliptin-associated risk for major birth defects and miscarriage. Published studies with metformin use during pregnancy have not reported a clear association with metformin and major birth defect or miscarriage risk. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRAJENTA DUO® and any potential adverse effects on the breastfed child from TRAJENTA DUO® or from the underlying maternal condition. **Contraindications:** Severe renal impairment; Acute or chronic metabolic acidosis, including diabetic ketoacidosis; History of hypersensitivity reaction to linagliptin or metformin. **Special warnings and precautions:** Lactic acidosis is a rare, but serious, complication that can occur due to metformin accumulation. The risk increases with conditions such as renal impairment, sepsis, dehydration, excess alcohol intake, hepatic impairment, and acute congestive heart failure. If acidosis is suspected, TRAJENTA DUO® should be discontinued and the patient hospitalized immediately. In addition, TRAJENTA DUO® should be temporarily discontinued prior to any intravascular radiocontrast study and for any surgical procedure necessitating restricted intake of food or fluids. It should generally be avoided in patients with clinical or laboratory evidence of hepatic disease. It is contraindicated in patients with renal impairment. Before initiation of therapy with TRAJENTA DUO® and at least annually thereafter, renal function should be assessed and verified to be normal. If pancreatitis is suspected, promptly discontinue TRAJENTA DUO® and initiate appropriate management. An association between DPP-4 inhibitor treatment and heart failure has been observed in cardiovascular outcomes trials for two other members of the DPP-4 inhibitor class. Consider the risks and benefits of TRAJENTA DUO® prior to initiating treatment in patients at risk for heart failure. If heart failure develops, evaluate, and manage according to current standards of care and consider discontinuation of TRAJENTA DUO®. No conclusive evidence of macrovascular risk reduction with linagliptin or metformin. **Adverse reactions:** Adverse reactions reported in >5% of patients treated with TRAJENTA DUO® and greater than with placebo are nasopharyngitis and diarrhea. The use of linagliptin in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin was associated with a higher rate of hypoglycemia compared with placebo in clinical trials. Metformin may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with TRAJENTA DUO®. There have been post marketing reports of hypersensitivity reactions and acute pancreatitis, hypersensitivity reactions, rash, severe and disabling arthralgia, bullous

pemphigoid, stomatitis, rhabdomyolysis with linagliptin, and of liver injury with metformin.
Shelf Life: 18 Months. **Storage**: Store below 30°C. Store in the original package at a safe place out of the reach of children.

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