Prescribing Information

Xultophy®
Insulin degludec and Liraglutide.

Xultophy® is a pre-filled dial-a-dose pen. 1 mL solution contains 100 units insulin degludec and 3.6 mg liraglutide. One pre-filled pen contains 3 mL equivalent to 300 units insulin degludec and 10.8 mg liraglutide. One dose step contains 1 unit of insulin degludec and 0.036 mg of liraglutide.

Indication: Xultophy® is indicated for the treatment of adults with type 2 diabetes mellitus to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with basal insulin do not provide adequate glycaemic control.

Posology and administration: Basal insulin should be discontinued prior to initiation of Xultophy® and the dose of sulphonylurea should be considered. Therapy with basal insulin should be discontinued prior to initiation of Xultophy®. When transferring from basal insulin therapy, the recommended starting dose of Xultophy® is 16 dose steps (16 units insulin degludec and 0.6 mg liraglutide). The recommended starting dose should not be exceeded.

Close glucose monitoring is recommended during the transfer and in the following weeks. Xultophy® can be used in elderly patients. Glucose monitoring is to be intensified and the dose adjusted on an individual basis. The therapeutic experience in patients ≥75 years of age is limited. When Xultophy® is used in patients with mild renal impairment, glucose monitoring is to be intensified and the dose adjusted on an individual basis. Xultophy® cannot be recommended for use in patients with moderate or severe renal impairment including patients with end-stage renal disease. The therapeutic experience with Xultophy® in patients with hepatic impairment is currently too limited to recommend the use in these patients. There is no relevant use of Xultophy® in the paediatric population. Xultophy® is for subcutaneous use only. Xultophy® must not be administered intravenously or intramuscularly. Xultophy® is administered subcutaneously by injection in the thigh, the upper arm or the abdomen. Injection sites are always to be rotated.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special warnings and precautions for use:

Xultophy® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Hypoglycaemia may occur if the dose of Xultophy® is higher than required. Omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia. In combination with sulphonylurea, the risk of hypoglycaemia may be lowered by a reduction in the dose of sulphonylurea. Concomitant diseases in the kidney, liver or diseases affecting the adrenal, pituitary or thyroid gland may require changes of the Xultophy® dose. Patients whose blood-glucose control is greatly improved (e.g. by intensified therapy) may experience a change in their usual warning symptoms of hypoglycaemia, and must be advised accordingly. Usual warning symptoms of hypoglycaemia may disappear in patients with long-standing diabetes. If prolonged effect of Xultophy® may delay recovery from hypoglycaemia. Inadequate dosing and/or discontinuation of anti-diabetic treatment may lead to hyperglycaemia. In case of discontinuation of Xultophy®, ensure that instruction for initiation of alternative anti-diabetic medication is followed. Furthermore, concomitant illness, especially infections, may aggravate hyperglycaemia and thereby cause an increased requirement for anti-diabetic treatment. Administration of rapid-acting insulin should be considered in situations of severe hyperglycaemia. Untreated hyperglycaemia events eventually lead to hyperosmolar coma/diabetic ketoacidosis, which is potentially lethal. Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin medicinal products, especially in patients with risk factors for development of cardiac failure. If the combination of pioglitazone and Xultophy® is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac function occurs. Intensified treatment with insulin, a component of Xultophy®, with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy, while long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy.

Administration of Xultophy® may cause formation of antibodies against insulin degludec and/or liraglutide. In rare cases, the presence of such antibodies may necessitate adjustment of the Xultophy® dose in order to correct a tendency to hyper- or hypoglycaemia. Very few patients developed insulin degludec specific antibodies, antibodies cross-reacting to human insulin or anti-liraglutide antibodies following treatment with Xultophy®. Antibody formation has not been associated with reduced efficacy of Xultophy®. Use of GLP-1 receptor agonists including liraglutide, a component of Xultophy®, has been associated with a risk of developing acute pancreatitis. There have been few reported events of acute pancreatitis. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Xultophy® should be discontinued; if acute pancreatitis is confirmed, Xultophy® should not be restarted. Caution should be exercised in patients with a history of pancreatitis. Thyroid adverse events, including increased blood calcitonin, goitre and thyroid neoplasm have been reported in clinical trials with GLP-1 receptor agonists including liraglutide, a component of Xultophy®, in particular in patients with pre-existing thyroid disease, and Xultophy® should therefore be used with caution. There is no experience with Xultophy® in patients with inflammatory bowel disease and diabetic gastroparesis. Xultophy® is therefore not recommended in these patients. Signs and symptoms of dehydration, including renal impairment and acute renal failure have been reported in clinical trials with GLP-1 receptor agonists including liraglutide, a component of Xultophy®, in particular in patients with pre-existing thyroid disease, and Xultophy® should therefore be used with caution. There is no experience with Xultophy® in patients with inflammatory bowel disease and diabetic gastroparesis. Xultophy® is therefore not recommended in these patients.
dipeptidyl peptidase 4 (DPP-4) inhibitors, glinides or prandial insulin. There is limited experience in patients with congestive heart failure New York Heart Association (NYHA) class I-II and Xultophy® should therefore be used with caution. There is no experience in patients with congestive heart failure NYHA class III-IV and Xultophy® is therefore not recommended in these patients.

**Fertility, pregnancy and lactation:**
If a patient wishes to become pregnant, pregnancy occurs or is breast feeding; treatment with Xultophy® should be discontinued. Animal reproduction studies with insulin degludec or liraglutide have not revealed any adverse effects on fertility.

**Undesirable effects:**
Adverse reactions associated with Xultophy® are given below, listed by system organ class and frequency. Very common (≥1/10): Hypoglycaemia. Common (≥1/100 to <1/10): Decreased appetite, nausea, diarrhoea, vomiting, constipation, dyspepsia, gastritis, abdominal pain, flatulence, gastroesophageal reflux disease, abdominal distension and injection site reactions. Uncommon (≥1/1,000 to <1/100): Urticaria, anaphylactic reactions, dehydration, rash, pruritus and increased heart. Rare (≥1/10,000 to <1/1,000): Hypersensitivity, lipodystrophy acquired. The Summary of Product Characteristics should be consulted for a full list of side effects.

**MA numbers and Basic NHS Price:**
EU/1/14/947/003
£159.22; 5 x 3 ml 100 U/mL
Xultophy® pre-filled dial-a-dose pen.

**Legal category:** POM.

**Full prescribing information can be obtained from:**
Novo Nordisk Limited, 3 City Place, Beehive Ring Road, Gatwick, West Sussex, RH6 0PA.

**Marketing Authorisation Holder:** Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.

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