

### Xultophy<sup>®</sup> 100/3.6 (insulin degludec/liraglutide) – New Drug Approval

- On November 21, 2016, [Novo Nordisk announced](#) the FDA approval of [Xultophy 100/3.6 \(insulin degludec/liraglutide\)](#) as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) inadequately controlled on basal insulin (< 50 units daily) or liraglutide (≤ 1.8 mg daily).
  - Xultophy is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans.
  - Xultophy has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
  - Xultophy is not recommended for use in combination with any other product containing liraglutide or another glucagon-like peptide 1 receptor agonist (GLP-1 RA).
  - Xultophy is not indicated for use in patients with type 1 diabetes mellitus (T1DM) or for the treatment of diabetic ketoacidosis.
  - Xultophy has not been studied in combination with prandial insulin.
- Xultophy is a once-daily, single injection fixed combination of a long-acting basal insulin analog, [Tresiba<sup>®</sup> \(insulin degludec\)](#), and a GLP-1 RA, [Victoza<sup>®</sup> \(liraglutide\)](#).
- The safety and efficacy of Xultophy were based on data from three randomized clinical trials involving 1,393 T2DM patients who were inadequately controlled on liraglutide or basal insulin therapy and switched to Xultophy. Patients may have received oral antidiabetic (OAD) therapy during the study. The primary endpoint was a reduction in HbA1C from baseline to week 26.
  - In a study comparing Xultophy + OADs vs. liraglutide + OADs, there was a reduction in baseline HbA1C of -1.31% for Xultophy and -0.36% for liraglutide (p < 0.0001 for superiority).
  - In a study comparing Xultophy + metformin vs. insulin degludec + metformin, the reduction in baseline HbA1C was -1.94% with Xultophy and -1.05% with insulin degludec (p < 0.01). This trial was designed to show the contribution of liraglutide to glycemic lowering and may not reflect real world clinical practice.
  - In a study comparing Xultophy + metformin vs. insulin glargine + metformin, the reduction in baseline HbA1C was -1.67% with Xultophy and -1.16% with insulin glargine (p < 0.01 for non-inferiority).
- Xultophy carries a boxed warning for risk of thyroid c-cell tumors.
- Xultophy is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2 and during episodes of hypoglycemia.
- Other warnings and precautions of Xultophy include pancreatitis, hyperglycemia/hypoglycemia with changes in Xultophy regimen, overdose due to medication errors, acute kidney injury, hypersensitivity and allergic reactions, hypokalemia, fluid retention and congestive heart failure with concomitant use of a peroxisome proliferator-activated receptor (PPAR)-gamma agonist, and lack of macrovascular outcomes data. Xultophy should never be shared between patients, even if the needle is changed.

- The most common adverse reactions ( $\geq 5\%$ ) with Xultophy use were nasopharyngitis, headache, nausea, diarrhea, increased lipase, and upper respiratory tract infection.
- Liraglutide or basal insulin should be discontinued prior to initiation of Xultophy therapy.
- The recommended starting dose of Xultophy is 16 units (16 units of insulin degludec/0.58 mg of liraglutide) given subcutaneously to the thigh, upper arm, or abdomen once daily at the same time each day.
  - The maximum daily dose is 50 units (50 units of insulin degludec/1.8 mg of liraglutide).
  - Xultophy delivers doses from 10 to 50 units with each injection; each Xultophy dosage unit contains 1 unit of insulin degludec and 0.036 mg of liraglutide.
  - Alternative antidiabetic products should be used if patients require a Xultophy daily dosage persistently  $< 16$  units or  $> 50$  units.
  - Refer to the prescribing information for specific titration instructions.
- Novo Nordisk plans to launch Xultophy 100/3.6 in the first half of 2017. Xultophy will be available as a 3 mL single-patient-use pen containing 100 units of insulin degludec and 3.6 mg of liraglutide per mL.



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