Xultophy® 100/3.6 (insulin degludec and liraglutide injection) – Expanded indication

- On February 27, 2019, the FDA approved Novo Nordisk's Xultophy 100/3.6 (insulin degludec and liraglutide), as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
    - Previously, Xultophy was approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (less than 50 units daily) or Victoza® (liraglutide) (less than or equal to 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 is not recommended for use in combination with any other product containing liraglutide or another glucagon-like peptide 1 (GLP-1) receptor agonist.
    - Xultophy is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
    - Xultophy has not been studied in combination with prandial insulin.

- The approval of Xultophy's expanded indication was based on two, 26-week studies in patients with type 2 diabetes inadequately controlled on one or more oral antidiabetic drugs. Study 1 (N = 1,660) was open-label and patients were randomized to Xultophy, Tresiba® (insulin degludec), or Victoza. Study 2 (N = 435) was double-blind and patients were randomized to Xultophy or placebo.
    - In study 1, treatment with Xultophy, Tresiba, and Victoza resulted in a reduction in HbA1c from baseline of 1.81%, 1.35% and 1.21%, respectively. The estimated difference between Xultophy and Tresiba was -0.46% (95% CI: -0.59, -0.34; $p < 0.01$ for non-inferiority). The estimated difference between Xultophy and Victoza was -0.60% (95% CI: -0.72, -0.47; $p < 0.01$ for superiority).
    - In study 2, treatment with Xultophy resulted in statistically significant reductions in HbA1c vs. placebo (estimated treatment difference: -0.81%; 95% CI: -0.98; -0.63; $p < 0.01$ superiority).

- Xultophy carries a boxed warning for risk of thyroid C-cell tumors.

- The recommended starting dose of Xultophy in patients naïve to basal insulin or GLP-1 receptor agonists is 10 units (10 units of insulin degludec and 0.36 mg of liraglutide) given subcutaneously (SC) once daily.

- The recommended starting dose of Xultophy in patients currently on basal insulin or GLP-1 receptor agonists is 16 units (16 units of insulin degludec and 0.58 mg of liraglutide) given SC once-daily.
    - Xultophy should be administered at the same time each day with or without food.
    - The maximum daily dosage of Xultophy is 50 units (50 units of insulin degludec and 1.8 mg of liraglutide).
    - Xultophy delivers doses from 10 to 50 units with each injection.
    - Refer to the Xultophy drug label for specific titration instructions.