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

XULTOPHY® 100/3.6 REMS
(Risk Evaluation and Mitigation Strategy)

FDA Required REMS* Safety Information

- **Potential Risk of Medullary Thyroid Carcinoma**
- **Risk of Acute Pancreatitis**

Potential Risk of Medullary Thyroid Carcinoma

BOXED WARNING- Risk of Thyroid C-Cell Tumors*

- Liraglutide, one of the components of XULTOPHY® 100/3.6, causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether XULTOPHY® 100/3.6 causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.
- XULTOPHY® 100/3.6 is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2).

- Cases of MTC in patients treated with liraglutide have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and liraglutide use in humans.
- **Counsel patients** regarding the risk of MTC and the symptoms of thyroid tumors (e.g., **mass in the neck, dysphagia, dyspnea or persistent hoarseness**). Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.
- Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with XULTOPHY® 100/3.6. Such monitoring may increase the risk of unnecessary procedures, due to the low specificity of serum calcitonin testing for MTC and a high background incidence of thyroid disease. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated.

* The information presented in this box does not represent the complete Boxed Warning. Please see the Prescribing Information.

Risk of Acute Pancreatitis

- Based on spontaneous postmarketing reports, **acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with liraglutide**.
- After initiation of XULTOPHY® 100/3.6, and after dose increases, **observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting).**
- Discontinue XULTOPHY® 100/3.6 if pancreatitis is suspected. Do not restart if pancreatitis is confirmed.
- Consider other antidiabetic therapies in patients with a history of pancreatitis.
- XULTOPHY® 100/3.6 has not been studied in patients with a history of pancreatitis.

Indication: XULTOPHY® 100/3.6 is a combination of insulin degludec and liraglutide, indicated 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 liraglutide (less than or equal to 1.8 mg daily).

XULTOPHY®100/3.6 is not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.

* What is the XULTOPHY® 100/3.6 REMS?

- A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. FDA has determined that a REMS is necessary to ensure that the benefits of XULTOPHY® 100/3.6 outweigh the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis. Novo Nordisk Inc. has established an informational program for healthcare professionals to help minimize these risks. This factsheet is required by the FDA as part of the XULTOPHY® 100/3.6 REMS program.
- Please visit www.xultophy10036pro.com/REMS for further information.

Reporting Adverse Events:

To report adverse events contact:

- Novo Nordisk at 1-800-727-6500 and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This factsheet does not contain the complete safety profile for XULTOPHY® 100/3.6. Please refer to the Prescribing Information, including Boxed Warning, for further information. If you have any questions about these materials, please call the Novo Nordisk Customer Care Center at 1-800-727-6500.