

## press release

### **Novo Nordisk Receives FDA Approval for Xultophy® 100/3.6 (insulin degludec and liraglutide injection)**

***New combination therapy offers reductions in A1C for adults with Type 2 diabetes who are inadequately controlled on basal insulin (less than 50 units) daily or liraglutide (less than or equal to 1.8 mg) daily***

**Plainsboro, N.J. (November 21, 2016)** – Novo Nordisk, a world leader in diabetes care, today announced that the U.S. Food and Drug Administration (FDA) approved the New Drug Application for Xultophy® 100/3.6 (insulin degludec 100 units/mL and liraglutide 3.6 mg/mL injection). Xultophy® 100/3.6 is a once-daily, combination of Tresiba® (insulin degludec injection) and Victoza® (liraglutide) injection indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes inadequately controlled on less than 50 units of basal insulin daily or less than or equal to 1.8 mg of liraglutide daily.<sup>1</sup> Xultophy® 100/3.6 enters into a new class of diabetes treatments that combine a basal insulin and a glucagon-like peptide-1 receptor agonist (GLP-1 RA) in a single, once-daily injection.

“Novo Nordisk is committed to discovering and developing new medicines, like Xultophy® 100/3.6, that may make a difference in the way some adults with type 2 diabetes manage their diabetes and achieve their treatment goals,” said Jakob Riis, executive vice president and head of North America Operations, Novo Nordisk A/S. “Combining Tresiba® and Victoza® into a single injection will offer patients a new option that may help control their blood sugar. We look forward to making Xultophy® 100/3.6 available to adults with type 2 diabetes in the first half of 2017.”

The approval of Xultophy® 100/3.6 is based on efficacy and safety data from the DUAL™ (Dual Action of Liraglutide and Insulin Degludec in Type 2 Diabetes) clinical development program. In three DUAL™ trials involving 1,393 adults with type 2 diabetes, patients who were inadequately controlled on liraglutide or basal insulin therapy and switched to Xultophy® 100/3.6 achieved reductions in A1C.<sup>2,3</sup> For adults uncontrolled on basal insulin, Xultophy® 100/3.6 demonstrated significant reductions in A1C from baseline of 1.67% and 1.94%.<sup>2,4</sup>

**Please see next page for Important Safety Information.**

The most common adverse events seen during the DUAL™ clinical development program included nasopharyngitis, headache, nausea, diarrhea, increased lipase, and upper respiratory tract infection.<sup>2,4</sup>

Novo Nordisk expects to launch Xultophy® 100/3.6 (insulin degludec and liraglutide injection) in the U.S. in the first half of 2017. Novo Nordisk will work diligently to secure access for Xultophy® 100/3.6 on health plans nationwide and is committed to ensuring that Xultophy® 100/3.6 is accessible and affordable for all appropriate patients. Novo Nordisk will also offer a savings card that will allow eligible patients with commercial insurance to reduce their co-pay.

"I am excited for this new class of type 2 diabetes medication that can offer patients another treatment option to help them reach their goals," said Professor John Buse, M.D., University of North Carolina School of Medicine, Chapel Hill, NC, and principal investigator for DUAL™ II. According to Buse, in the clinical development program, Xultophy® 100/3.6 showed improved glycemic control in patients who were uncontrolled on either liraglutide or basal insulin therapy.

Xultophy® 100/3.6 is administered as a once-daily injection from a prefilled pen and can be taken with or without food. Each Xultophy® 100/3.6 dosage unit contains one unit of insulin degludec and 0.036 mg of liraglutide.<sup>1</sup> The starting dose of Xultophy® 100/3.6 is 16 units (16 units insulin degludec and 0.58 mg liraglutide).<sup>1</sup> The maximum dose of 50 units of Xultophy® 100/3.6 corresponds to 50 units of insulin degludec and 1.8 mg of liraglutide.<sup>1</sup>

## **Medication Guide**

### **XULTOPHY® 100/3.6 (ZUL-to-fye) (insulin degludec and liraglutide injection) for subcutaneous injection**

Read this Medication Guide before you start using XULTOPHY 100/3.6 and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

### **What is the most important information I should know about XULTOPHY 100/3.6?**

#### **XULTOPHY 100/3.6 may cause serious side effects, including:**

- **Possible thyroid tumors, including cancer.** Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rats and mice, liraglutide, one of the components of XULTOPHY 100/3.6, and medicines that work like liraglutide caused thyroid tumors, including thyroid cancer. It is not known if XULTOPHY 100/3.6 will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.
- Do not use XULTOPHY 100/3.6 if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an

endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

### **What is XULTOPHY 100/3.6?**

XULTOPHY 100/3.6 is an injectable prescription medicine that contains 2 diabetes medicines, insulin degludec, 100 units/mL, and liraglutide, 3.6 mg/mL. XULTOPHY 100/3.6 should be used along with diet and exercise to lower blood sugar (glucose) in adults with type 2 diabetes mellitus when blood sugar levels are not well controlled on: 1) basal insulin (less than 50 units daily) or 2) liraglutide (less than or equal to 1.8 mg daily).

- XULTOPHY 100/3.6 is not recommended as the first choice of medicine for treating diabetes.
- It is not known if XULTOPHY 100/3.6 can be used in people who have had pancreatitis.
- XULTOPHY 100/3.6 is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.
- XULTOPHY 100/3.6 is not for use in people with type 1 diabetes or people with diabetic ketoacidosis (increased ketones in the blood or urine).
- It is not known if XULTOPHY 100/3.6 can be used with mealtime insulin.
- It is not known if XULTOPHY 100/3.6 is safe and effective for use in children under 18 years of age.

### **Who should not use XULTOPHY 100/3.6?**

#### **Do not use XULTOPHY 100/3.6 if:**

- you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- you are allergic to insulin degludec, liraglutide or any of the ingredients in XULTOPHY 100/3.6. See the end of this Medication Guide for a complete list of ingredients in XULTOPHY 100/3.6.
- you are having an episode of low blood sugar (hypoglycemia).

### **What should I tell my healthcare provider before using XULTOPHY 100/3.6?**

#### **Before using XULTOPHY 100/3.6, tell your healthcare provider about all your medical conditions, including if you:**

- have or have had problems with your pancreas, kidneys, or liver.
- have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.
- are taking certain medicines called glucagon-like peptide 1 receptor agonists (GLP-1 receptor agonists).
- are pregnant or plan to become pregnant. It is not known if XULTOPHY 100/3.6 will harm your unborn baby. Tell your healthcare provider if you become pregnant while using XULTOPHY 100/3.6.
- are breastfeeding or plan to breastfeed. It is not known if XULTOPHY 100/3.6 passes into your breast milk. You should not use XULTOPHY 100/3.6 while breastfeeding.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

XULTOPHY 100/3.6 may affect the way some medicines work and some medicines may affect the way XULTOPHY 100/3.6 works. **Before using XULTOPHY 100/3.6, talk to your healthcare provider about low blood sugar and how to manage it.** Tell your healthcare provider if you are taking other medicines to treat diabetes.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

### **How should I use XULTOPHY 100/3.6?**

- Read the **Instructions for Use** that comes with XULTOPHY 100/3.6.
- Use XULTOPHY 100/3.6 exactly as your healthcare provider tells you to.
- Do not change your dosing schedule without first talking to your healthcare provider. The dose counter on your XULTOPHY 100/3.6 pen shows the number of units of XULTOPHY 100/3.6 to be injected.
- **Your healthcare provider should show you how to use XULTOPHY 100/3.6 before you use it for the first time.**
- XULTOPHY 100/3.6 is injected under the skin (subcutaneously) of your thigh, upper arm or stomach (abdomen).
- **Do not** inject XULTOPHY 100/3.6 into a muscle (intramuscularly) or vein (intravenously).
- **Use XULTOPHY 100/3.6 at the same time each day with or without food.**
- If you miss a dose of XULTOPHY 100/3.6, resume your 1 time daily dosing schedule at the next scheduled dose. Do not take 2 doses at the same time or increase your dose to make up for the missed dose. If you miss more than 3 days of XULTOPHY 100/3.6, call your healthcare provider for further instructions about taking XULTOPHY 100/3.6 at the right dose and to help lower your chance of having an upset stomach.
- Do not mix XULTOPHY 100/3.6 with any other insulin products or GLP-1 receptor agonists in the same injection.
- Check the Pen label each time you give your injection to make sure you are using the correct medication.
- **Do not take more than 50 units of XULTOPHY 100/3.6 each day.** XULTOPHY 100/3.6 contains two medicines: insulin degludec and liraglutide. If you take too much XULTOPHY 100/3.6, it can cause severe nausea and vomiting. Do not take XULTOPHY 100/3.6 with other GLP-1 receptor agonists. If you take too much XULTOPHY 100/3.6, call your healthcare provider or go to the nearest hospital emergency room right away.
- Change (rotate) your injection site with each injection to help reduce your chances of getting skin thickening or pits at the injection site. **Do not** use the same site for each injection.
- **Do not share your XULTOPHY 100/3.6 pen with other people, even if the needle has been changed.** You may give other people a serious infection or get a serious infection from them.

**Check your blood sugar levels.** Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.

**Your dose of XULTOPHY 100/3.6 and other diabetes medicines may need to change because of:**

- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

### **What should I avoid while taking XULTOPHY 100/3.6?**

#### **While taking XULTOPHY 100/3.6 do not:**

- drive or operate heavy machinery, until you know how XULTOPHY 100/3.6 affects you.
- drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

### **What are the possible side effects of XULTOPHY 100/3.6?**

#### **XULTOPHY 100/3.6 may cause serious side effects that can lead to death, including:**

- **See "What is the most important information I should know about XULTOPHY 100/3.6?"**
- **inflammation of your pancreas (pancreatitis).** Stop using XULTOPHY 100/3.6 and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.
- **low blood sugar (hypoglycemia).** Your risk for getting low blood sugar may be higher if you use XULTOPHY 100/3.6 with another medicine that can cause low blood sugar.

#### **Signs and symptoms of low blood sugar may include:**

- |                                 |                  |  |
|---------------------------------|------------------|--|
| • dizziness or light-headedness | • blurred vision | • anxiety, irritability, or mood changes |
| • sweating                      | • slurred speech | • hunger                                 |
| • confusion or drowsiness       | • shakiness      | • weakness                               |
| • headache                      | • fast heartbeat | • feeling jittery                        |
- **kidney problems (kidney failure).** In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.
  - **serious allergic reactions.** Stop using XULTOPHY 100/3.6 and get medical help right away, if you have any symptoms of a serious allergic reaction including itching, rash, or difficulty breathing.
  - **heart failure.** Taking certain diabetes medicines called peroxisome proliferator-activated receptor (PPAR) gamma agonists or PPAR agonists with insulin containing products, including XULTOPHY 100/3.6, may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure, it may get worse while you take PPAR agonists with XULTOPHY 100/3.6. Your healthcare provider should monitor you closely while you are taking PPAR agonists with XULTOPHY 100/3.6. Tell your healthcare provider if you have any new or worse symptoms of heart failure including shortness of breath, tiredness, swelling of your ankles or feet and sudden weight gain. Treatment with PPAR agonists and XULTOPHY 100/3.6 may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.
  - **low potassium in your blood (hypokalemia)**

**The most common side effects of XULTOPHY 100/3.6 may include** stuffy or runny nose, sore throat, upper respiratory tract infection, increased blood levels of lipase,

nausea, diarrhea, and headache. Talk to your healthcare provider about any side effect that bothers you or does not go away.

These are not all the possible side effects of XULTOPHY 100/3.6.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Keep XULTOPHY 100/3.6 and all medicines out of the reach of children.

### **General information about the safe and effective use of XULTOPHY 100/3.6.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use XULTOPHY 100/3.6 for a condition for which it was not prescribed. Do not give XULTOPHY 100/3.6 to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about XULTOPHY 100/3.6 that is written for healthcare professionals.

### **What are the ingredients in XULTOPHY 100/3.6?**

**Active Ingredients:** insulin degludec and liraglutide

**Inactive Ingredients:** glycerol, phenol, zinc, and water for injection

### **Manufactured by:**

Novo Nordisk A/S

DK-2880 Bagsvaerd, Denmark

For more information, go to [www.novonordisk-us.com](http://www.novonordisk-us.com) or call 1-800-727-6500.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Approved: November 2016

Please [click here](#) for Xultophy® 100/3.6 Prescribing Information, including Boxed Warning.

### **About Diabetes**

In the United States, more than 29 million people are affected by diabetes.<sup>5</sup> Type 2 diabetes accounts for 90 to 95 percent of all diabetes cases.<sup>5</sup> Diabetes is emerging as one of the most serious health problems of our time; the number of Americans with diabetes has quadrupled over the past 30 years.<sup>6</sup>

### **About Novo Nordisk**

*Novo Nordisk is a global healthcare company with more than 90 years of innovation and leadership in diabetes care. This heritage has given us experience and capabilities that also enable us to help people defeat other serious chronic conditions: hemophilia, growth disorders and obesity. Headquartered in Denmark, Novo Nordisk employs approximately 41,600 people in 75 countries and markets its products in more than 180 countries. For more information, visit [novonordisk-us.com](http://novonordisk-us.com) or follow us on Twitter: @novonordiskus.*

**For further information**

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