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.
- XULTOPHY 100/3.6 is not recommended as the first choice of medicine for treating diabetes.
- XULTOPHY 100/3.6 is not recommended for use in combination with any other product containing liraglutide or another glucagon-like peptide 1 receptor agonist (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.

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 having an episode of low blood sugar (hypoglycemia).
- 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.

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 heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with XULTOPHY 100/3.6.
- have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.
- are taking certain medicines called GLP-1 receptor agonists.
- have had an allergic reaction to a GLP-1 receptor agonist medicine.
- 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 or think you may be 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. Talk to your healthcare provider about the best way to feed your baby while using XULTOPHY 100/3.6.

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 vein (intravenously) or use in an insulin infusion pump.
- **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 dilute XULTOPHY 100/3.6 with any other liquids.
- Do not mix XULTOPHY 100/3.6 with any other insulin products or GLP-1 receptor agonists in the same injection.
- Do not split your dose of XULTOPHY 100/3.6. Give your full dose of XULTOPHY 100/3.6 in 1 injection.
- Check the Pen label each time you give your injection to make sure you are using the correct medicine.
- **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 sites within the area you choose with each injection** to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.
  - **Do not** use the exact same spot for each injection.
  - **Do not** inject where the skin has pits, is thickened, or has lumps.
  - **Do not** inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.
- **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:

- o dizziness or light-headedness
- o sweating
- o confusion or drowsiness
- o headache
- o blurred vision
- o slurred speech
- o shakiness
- o fast heartbeat
- o anxiety, irritability, or mood changes
- o hunger
- o weakness
- o feeling jittery

- **kidney problems (kidney failure).** Worsening of kidney failure and sudden kidney failure have happened in people with kidney problems and in people without kidney problems, who have taken liraglutide, one of the ingredients in XULTOPHY 100/3.6. Diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse. Tell your healthcare provider if you have diarrhea, nausea, or vomiting. Drink plenty of fluids to help reduce your risk of dehydration during treatment with XULTOPHY 100/3.6.
- **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:
  - o hives
  - o rash
  - o itching
  - o fast heartbeat
  - o fainting or feeling dizzy
  - o swelling of your face, lips, tongue, or throat
  - o problems breathing or swallowing
  - o sudden coughing
  - o chest pain or tightness
- **gallbladder problems.** Gallbladder problems have happened in some people who take XULTOPHY 100/3.6. Tell your healthcare provider right away if you get symptoms of gallbladder problems which may include:
  - o pain in your upper stomach (abdomen)
  - o fever
  - o yellowing of skin or eyes (jaundice)
  - o clay-colored stools
- **low potassium in your blood (hypokalemia).**
- **heart failure.** Taking certain diabetes pills called thiazolidinediones or TZDs with 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 TZDs with XULTOPHY 100/3.6. Your healthcare provider should monitor you closely while you are taking TZDs 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 TZDs and XULTOPHY 100/3.6 may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.

The most common side effects of XULTOPHY 100/3.6 include stuffy or runny nose, sore throat, headache, nausea, diarrhea, increased blood levels of lipase, and upper respiratory tract infection. 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 health 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. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

Manufactured by: Novo Nordisk Inc., Plainsboro, NJ 08536, U.S. License Number 1261
For more information, go to www.novonordisk-us.com or call 1-800-727-6500 (Se habla español).
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