Xultophy 100/3.6
(insulin degludec, liraglutide)
Introduction

- **Brand name:** Xultophy
- **Generic name:** Insulin degludec, liraglutide
- **Pharmacological class:** Human insulin analog + glucagon-like peptide-1 receptor agonist
- **Strength and Formulation:** Insulin degludec 100 Units/mL, liraglutide 3.6mg/mL; solution for SC injection
- **Manufacturer:** Novo Nordisk
- **How supplied:** Single-use prefilled pen (3mL)—5
- **Legal Classification:** Rx
XULTOPHY 100/3.6

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

For Single Patient Use Only
100 units/ml and 3.6 mg/ml

NDC 0169-2911-15 List: 291115
Indications

- As adjunct to diet and exercise, to improve glycemic control in adults with **type 2 diabetes mellitus** inadequately controlled on basal insulin (<50 Units daily) or liraglutide (≤1.8mg daily)
Limitations of Use

- **Not** recommended as first-line treatment for patients inadequately controlled on diet and exercise
- **Not** studied in patients with history of pancreatitis; consider other antidiabetics
- **Not** for use with other liraglutide- or GLP-1 receptor agonist-containing products
- **Not** for treating type 1 diabetes mellitus or diabetic ketoacidosis
- **Not** studied in combination with prandial insulin
**Dosage & Administration**

- **Discontinue** liraglutide or basal insulin prior to initiation

- Give by SC inj once daily at the same time each day into thigh, upper arm or abdomen; rotate inj sites

- Individualize; monitor and adjust as needed

- Initially 16 Units once daily
Dosage & Administration

- Titrate dose by 2 Units every 3–4 days until desired FPG achieved; max 50 Units
- If persistently <16 Units or >50 Units daily required: use alternative antidiabetic products
- Switching from basal insulin or liraglutide: see full labeling
Considerations for Special Populations

- **Pregnancy:** Use only if potential benefit justifies potential risk to fetus
- **Nursing mothers:** Consider mother’s clinical need and any potential adverse effects on infant
- **Pediatric:** Not established
- **Elderly:** Dosing should be conservative to avoid hypoglycemic reactions
- **Renal impairment:** Monitor and avoid fluid depletion
Contraindications

- History (personal or family) of medullary thyroid carcinoma
- Multiple endocrine neoplasia syndrome type 2
- During episodes of hypoglycemia
Warnings/Precautions

- **Risk of thyroid C-cell tumors;** inform patients of potential risk and symptoms

- Monitor for signs/symptoms of **pancreatitis;** discontinue if suspected; do not restart if confirmed

- Instruct patients on diet, exercise, blood testing, proper administration of insulin, and management of **hypoglycemia**

- **Do not** reuse or share pens or needles between patients
Increased risk of hypo- or hyperglycemia if changes in physical activity, meal patterns, renal or hepatic function, insulin regimen, and if acute illness occurs: monitor glucose more frequently and may need to adjust dose.

Monitor potassium levels in patients at risk for hypokalemia (eg, concomitant K⁺-lowering or K⁺-sensitive drugs).

Discontinue if hypersensitivity reactions occur.

Pre-existing gastroparesis.

GI adverse reactions: monitor and avoid fluid depletion.
**Interactions**

- **Do not** mix or dilute with other insulins or solutions

- Concomitant peroxisome proliferator-activated receptor (PPAR)-gamma agonists may cause fluid retention and heart failure; consider dose reduction or discontinue PPAR-gamma agonists
Increased **risk of hypoglycemia** with concomitant:

- Antidiabetics
- ACE inhibitors
- ARBs
- Disopyramide
- Fibrates
- Fluoxetine
- MAOIs
- Pentoxifylline
- Pramlintide
- Propoxyphene
- Salicylates
- Somatostatin analogs
- Sulfonamide antibiotics
**Interactions**

- **Reduced efficacy** with concomitant atypical antipsychotics, corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens, protease inhibitors, somatropin, sympathomimetics, thyroid hormones
Interactions

- Variable effects with β-blockers, clonidine, lithium salts, alcohol, pentamidine
- Concomitant β-blockers, clonidine, guanethididine, reserpine may blunt hypoglycemia
- May affect absorption of other drugs (delayed gastric emptying)
Adverse Reactions

- Nasopharyngitis
- Headache
- Nausea
- Diarrhea
- Increased lipase
- Upper respiratory tract infection
- Hypoglycemia
- Hypokalemia
- Lipodystrophy
- Acute kidney injury
- Pancreatitis
- Papillary thyroid carcinoma
- Anaphylactic reactions
- Angioedema
**Insulin** and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production.

Insulin also inhibits lipolysis and proteolysis, and enhances protein synthesis.

**Liraglutide** is a glucagon-like peptide-1 receptor agonist that increases glucose-dependent insulin release, decreases glucagon secretion, and slows gastric emptying.
Clinical Studies

- Three randomized, parallel and active-controlled Phase 3 studies lasting 26 weeks evaluated 1,933 patients with type 2 diabetes
  - **Study A** evaluated patients converting from liraglutide up to 1.8mg
  - **Study B** evaluated patients converting from any basal insulin
  - **Study C** evaluated patients converting from insulin glargine U-100
In **Study A**, Xultophy 100/3.6 was compared to unchanged pre-trial liraglutide up to 1.8mg daily in a 26-week, randomized, open-label, treat-to-target (FPG goal 72–90mg/dL) in 348 patients.

- Oral antidiabetics were continued at pre-trial doses throughout the trial:
  - 21.8% were treated with sulfonylureas with metformin with or without pioglitazone.
Clinical Studies

- The **primary endpoint** was the change in HbA1c tested for superiority between Xultophy 100/3.6 and unchanged liraglutide therapy.

- At the end of Week 26, there was a greater reduction in HbA1c from baseline for Xultophy 100/3.6 vs. liraglutide (-1.31% vs. -0.36%).
  - Estimated treatment difference (-0.95, 95% CI: -1.15, -0.75)
More patients in the Xultophy 100/3.6 group achieved HbA1c <7% vs. patients in the liraglutide group (74.6% vs. 30.2%)

At the end of trial, there was a greater change in least-squares mean FPG from baseline in the Xultophy 100/3.6 group vs. the liraglutide group (-51.1mg/dL vs. -10.9mg/dL)
In **Study B**, Xultophy 100/3.6 was compared to insulin degludec, both once daily added to metformin (n=398).

- Basal insulin and sulfonylureas/glinides were discontinued at randomization.
- The targeted FPG goal was achieved in 24.0% of patients randomized to insulin degludec vs. 31.6% of the patients randomized to Xultophy 100/3.6 at Week 26.
HbA1c reduction from baseline was -1.94% for the Xultophy 100/3.6 group vs. -1.05% for the insulin degludec group

- Estimated treatment difference (-0.89, 95% CI: -1.10, -0.68)

- More patients in the Xultophy 100/3.6 group achieved HbA1c <7% vs. patients in the insulin degludec group (57.3% vs. 22.6%)
In **Study C**, Xultophy 100/3.6 was compared to insulin glargine U-100, both once daily and added to metformin (n=557)

- The targeted FPG goal was achieved in 39.6% of patients randomized to insulin glargine vs. 32.9% of the patients randomized to Xultophy 100/3.6 at Week 26
HbA1c reduction from baseline was -1.67% for the Xultophy 100/3.6 group vs. -1.16% for the insulin glargine group

- Estimated treatment difference (-0.51, 95% CI: -0.67, -0.34)

More patients in the Xultophy 100/3.6 group achieved HbA1c <7% vs. patients in the insulin glargine group (68.3% vs. 46.2%)

For more clinical trial data, see full labeling
For more information view the product monograph available at:

http://www.empr.com/xultophy-10036/drug/34673/