Xultophy 100/3.6

(insulin degludec, liraglutide)

Xultophy® 100/3.6
insulin degludec 100 units/mL and
liraglutide 3.6 mg/mL injection

New Product
Slideshow

MPR

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

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

Warnings/Precautions

- 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

Interactions

- 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, guanethidine, 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

Mechanism of Action

- **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

Clinical Studies

- 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)

Clinical Studies

- 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**)

Clinical Studies

- 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

Clinical Studies

- 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%**)

Clinical Studies

- 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

Clinical Studies

- 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

New Product Monograph

- For more information view the product monograph available at:

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