Drug Monograph

Drug/Drug Class: **Trulicity™ (dulaglutide) injection/ GLP-1 receptor agonists**

Prepared for: MO HealthNet
Prepared by: Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Trulicity™ is available in a 0.75 mg/0.5 ml single-dose prefilled pen and a 1.5 mg/0.5 ml single-dose prefilled pen that contain 0.75 mg and 1.5 mg of dulaglutide respectively. Eli Lilly and Company Indianapolis, IN 46285
Summary of Findings:	Significant improvements in HbA1c were demonstrated in patients with type 2 diabetes treated with Trulicity™ in clinical trials. Once weekly doses of 0.75 mg or 1.5 mg resulted in HbA1c decreases of 0.71% and 0.78%, respectively, after 26 weeks of treatment and were noninferior to treatment with metformin. When used as add-on therapy in various trials, Trulicity™ was significantly better in improving HbA1c levels than exenatide or sitagliptin, and was noninferior to insulin glargine.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[4]

Type 2 diabetes, once called non-insulin-dependent diabetes, is the most common form of diabetes, affecting 90% to 95% of the 26 million Americans with diabetes.

Dosage Form(s) [1]

Trulicity™ is available in a 0.75 mg/0.5 ml single-dose prefilled pen and a 1.5 mg/0.5 ml single-dose prefilled pen that contain 0.75 mg and 1.5 mg of dulaglutide respectively.

Manufacturer [1]

Eli Lilly and Company, Indianapolis, IN 46285

Indication(s) [1]

Trulicity™ is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Clinical Efficacy [1,2,3] (mechanism of action/pharmacology, comparative efficacy)

Trulicity™ is a GLP-1 receptor agonist. Insulin release is stimulated in a glucose-dependent manner via activation of GLP-1 receptors on pancreatic beta cells. Trulicity™ is 90% homologous with endogenous human GLP-1. Glucagon secretion is also reduced and gastric emptying is delayed.

Pharmacokinetics

	Trulicity
Volume of distribution	17.4 to 19.2 L
Metabolism	Protein catabolism to component amino acids
Half-life	5 days

Trulicity ™ monotherapy was noninferior to metformin in improving HbA1c values among patients with inadequately controlled type 2 diabetes.

Trulicity™ Monotherapy

STUDY DESIGN	Randomized, double-blind, 52-week, noninferiority trial (n=807).
INCLUSION CRITERIA	Adults with type 2 diabetes inadequately controlled with diet and exercise, or receiving one oral antidiabetic agent (at no more than 50% of maximum doses) for at least 3 months.
EXCLUSION CRITERIA	Patients receiving thiazolidinediones, GLP-1 receptor agonists, or insulin.
TREATMENT REGIMEN	Patients were randomized to receive Trulicity™ 0.75 mg subQ once weekly (n=270), Trulicity™ 1.5 mg subQ once weekly (n=269), or oral metformin titrated up to 2000 mg daily (n=268).
RESULTS	At baseline, 75% of patients were receiving oral antidiabetic agents, of which 90% were receiving metformin. After 26 weeks of treatment, mean HbA1c values changed by -0.71% in the Trulicity™ 0.75 mg group, -0.78% in the Trulicity™ 1.5 mg group, and -0.56% in the metformin group. At 52 weeks, mean reductions were -0.55% and -0.7% with Trulicity™ 0.75 mg and 1.5 mg, respectively, compared with -0.51% with metformin. Both Trulicity™ doses were noninferior to metformin at 52 weeks. An HbA1c value of < 7% was achieved in 63%, 62%, and 54% of patients in the Trulicity™ 0.75 mg, 1.5 mg, and metformin groups, respectively, at 52 weeks. Patients in all 3 groups experienced weight loss.
SAFETY	The frequency of adverse events was similar in the 3 treatment groups, with gastrointestinal events being the most common.

Trulicity™ 0.75 mg and 1.5 mg once weekly reduced mean HbA1C significantly more than exenatide 10 mcg twice daily after 26 weeks of treatment when used as add-on therapy to metformin plus pioglitazone.

STUDY DESIGN	Randomized, 52-week, multicenter trial (n=976).
INCLUSION CRITERIA	Adults with type 2 diabetes inadequately controlled on oral antidiabetic therapy.
EXCLUSION CRITERIA	Patients receiving GLP-1 receptor agonists or insulin.
TREATMENT REGIMEN	All patients were treated with metformin (1500 to 3000 mg daily) and pioglitazone (30 to 45 mg daily) for up to 12 weeks and then continued for an 8-week stabilization period. Patients with an HbA1c > 6.5% were randomized to receive add-on therapy with Trulicity™ 0.75 mg subQ once

	weekly (n=280), Trulicity™ 1.5 mg subQ once weekly (n=279), exenatide 10 mcg subQ twice daily (titrated from 5 mcg twice daily; n=276), or placebo (n=141).
RESULTS	Trulicity™ 0.75 mg and 1.5 mg once weekly reduced mean HbA1C significantly more than exenatide 10 mcg twice daily after 26 weeks of treatment (-1.3% and -1.5% vs -1%). Superiority over exenatide was maintained after 52 weeks of treatment, with mean HbA1C reductions of -1.07% and -1.36% for Trulicity™ 0.75 mg and 1.5 mg, respectively, compared with -0.8% with exenatide. Weight reduction at 26 weeks was similar with Trulicity™ 1.5 mg (-1.3 kg) and exenatide (-1.07 kg), and was maintained at 52 weeks.
SAFETY	The frequency of adverse events was similar in the 3 treatment groups, with gastrointestinal events being the most common.

Contraindications [(1)]

- Hypersensitivity to Trulicity™ or any component of the product
- Medullary thyroid carcinoma, personal or family history
- Multiple endocrine neoplasia syndrome type 2

Warnings and Precautions [(1)]

- Thyroid C-cell tumors, increased risk possible; patients with thyroid nodules and/or elevated calcitonin levels should be referred to an endocrinologist; the value of routine monitoring has not been established.
- Gastrointestinal disease, preexisting and severe; use not recommended.
- Hypersensitivity reactions, systemic, have been reported; discontinue use immediately.
- Hypoglycemia, increased risk with concomitant use of insulin or insulin secretagogues (eg, sulfonylureas); consider reducing dose of insulin or insulin secretagogue when initiating Trulicity™.
- Pancreatitis has been reported; consider alternative therapy in patients with history of pancreatitis; monitoring recommended; if pancreatitis is suspected, suspend therapy immediately; if confirmed, permanently discontinue therapy.
- Renal failure, acute, or worsening of chronic renal failure has been reported in patients with or without underlying renal disease receiving other GLP-1 agonists.
- Renal impairment, use caution when initiating therapy, increasing dosage, and in patients experiencing severe gastrointestinal reactions; monitoring required.

Adverse Effects [1]

Most common, ≥ 5%	Trulicity™ (n=836)	Placebo (n=568)
Nausea	12.4%	5.3%
Diarrhea	8.9%	6.7%
Vomiting	6%	2.3%
Abdominal Pain	6.5%	4.9%
Decreased Appetite	4.9%	1.6%
Dyspepsia	4.1%	2.3%
Fatigue	4.2%	2.6%

Drug Interactions [1]

- Insulin
- Sulfonylureas: glipizide, glimepiride

Dosage and Administration [1]

The recommended initiating dose of Trulicity is 0.75 mg once weekly. The dose may be increased to 1.5 mg once weekly for additional glycemic control. Administer Trulicity any time of day, with or without food. Trulicity should be injected subcutaneously in the abdomen, thigh, or upper arm.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST*/ MONTH
Dulaglutide	Trulicity	Eli Lilly	0.75 mg/0.5 mL single-dose pen	0.75 mg once weekly	$585.98
			1.5 mg/0.5 mL single-dose pen	1.5 mg once weekly	$585.98
Albiglutide	Tanzeum	GlaxoSmithKline	30 mg/single-dose pen	30 mg once weekly	$391.15
			50 mg/single-dose pen	50 mg once weekly	$391.15
Liraglutide	Victoza	Novo Nordisk	6 mg/ml, 3 mL multi-dose prefilled pen	1.2 mg once daily	$470.88

*WholesaleAcquisitionCost

Conclusion

Trulicity™ is a subcutaneous GLP-1 receptor agonist approved for the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise. Trulicity™ demonstrated efficacy in the treatment of type 2 diabetes when used as monotherapy and in combination with various other antidiabetic agents. Once weekly doses of 0.75 mg or 1.5 mg resulted in HbA1c decreases of 0.71% and 0.78%, respectively, after 26 weeks of treatment and were noninferior to treatment with metformin. When used as add-on therapy in various trials, Trulicity™ was significantly better in improving HbA1c levels than exenatide or sitagliptin, and was noninferior to insulin glargine. Gastrointestinal adverse effects account for the most commonly reported toxicities. Trulicity™ is not recommended as first-line therapy, for treatment of type 1 diabetes mellitus or diabetic ketoacidosis, or for patients with preexisting severe gastrointestinal disease or a history of pancreatitis. It has not been studied with basal insulin.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List and is under solicitation.

References

1. Product Information: Trulicity™, dulaglutide injection. Eli Lilly and Company, Indianapolis, IN, 9/2014
2. Umpierrez G, Tofe Povedano S, Perez Manghi F et al: Efficacy and safety of dulaglutide monotherapy versus metformin in type 2 diabetes in a randomized controlled trial (AWARD-3). Diabetes Care 2014; 37(8):2168-2176.
3. Wysham C, Blevins T, Arakaki R et al: Efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes in a randomized controlled trial (AWARD-1). Diabetes Care 2014; 37(8):2159-2167.
4. Type 2 Diabetes Overview (2014). Retrieved March 3, 2015 from http://www.webmd.com/diabetes/guide/type-2-diabetes

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