PDL NEW DRUG REVIEW

Proprietary Name: Trulicity®
Common Name: dulaglutide
PDL Category: Diabetic, Non-Insulin Injectables

Comparable Products	Preferred Drug List Status
Byetta	Preferred with Conditions
Victoza	Non-Preferred with Conditions

Summary

Indications and Usage: Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Trulicity® is not recommended to be used as a first-line treatment for those who have inadequate glycemic control on diet and exercise. It should not be used in those with type 1 DM or for the treatment of diabetic ketoacidosis; it is not a substitute for insulin. The concurrent use with basal insulin has not been studied. Trulicity® has not been studied in those with a history of pancreatitis; thus, it is recommended to consider other antidiabetic therapies in this population. It has not been studied in those with severe GI disease, including gastroparesis; thus, use is not recommended in this population with pre-existing severe GI disease.

This is a pregnancy category C medication. The safety and efficacy of use in children have not been established.

Dosage Forms: Single-dose pen or prefilled syringe: 0.75mg/0.5ml, 1.5mg/0.5ml

Recommended Dosage: Administer 0.75mg SQ QW in the abdomen, thigh, or upper arm. Increase to a maximum of 1.5mg SQ QW if additional glycemic control is needed. When starting treatment, it is recommended to consider reducing the dose of concomitantly administered insulin secretagogues or insulin.

Dose adjustment is not recommended in those with renal or hepatic impairment. As there is limited clinical experience in those with hepatic impairment or in those with severe renal impairment or ESRD, it is recommended that treatment be used with caution in these patient populations. Renal function should be monitored in those with renal impairment reporting severe adverse GI reactions.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Trulicity® 0.75mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same or that the active drug was less than placebo.* The most frequently reported adverse events included nausea (7.1%), diarrhea (2.2%), vomiting (3.7%), abdominal pain (1.6%), decreased appetite (3.3%), dyspepsia (1.8%), fatigue (1.6%), constipation (3.2%), flatulence (0%), abdominal distension (2.2%), GERD (1.2%), eructation (0.4%), and hypoglycemia with add-on metformin (1.5%).

Contraindications: In those with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2); In those with a prior serious hypersensitivity reaction to dulaglutide or any component of the product

Manufacturer: Eli Lilly & Co

Analysis: Dulaglutide, the active ingredient of Trulicity®, is a human glucagon-like peptide (GLP-1) receptor agonist that increases cyclic AMP in beta cells; this leads to glucose-dependent insulin release. It also decreases glucagon secretion and slows gastric emptying. Trulicity® has a box warning regarding the increased risk of thyroid C-cell tumors, as it caused dose-related and treatment-duration dependent increases in the incidence of thyroid C-cell tumors in rats. Nevertheless, it is not known if it causes these tumors, including medullary thyroid carcinoma (MTC), in humans. The box warning also indicates that Trulicity® is contraindicated in those with a personal or family history of MTC and in those with MEN 2. It is recommended that all should be counseled on the risk factors and symptoms of thyroid tumors.

Several clinical trials were performed to assess the safety and efficacy of Trulicity®. One double-blind monotherapy trial compared both doses of Trulicity® with metformin. Changes in HbA1c were comparable between Trulicity® 0.75 and 1.5mg vs metformin (-0.7% and -0.8% vs -0.6%), as were changes in body weight (-2.3kg and -2.3kg vs -2.2kg). In an add-on to metformin study comparing Trulicity® with sitagliptin, treatment with Trulicity® 0.75mg and 1.5mg resulted in statistically significant reductions in HbA1c as compared to sitagliptin 100mg (-0.9% and -1.1% vs -0.4%) and compared with placebo. There was also greater weight change with both Trulicity® doses vs sitagliptin (-2.7kg and -3.1kg vs -1.5kg, respectively) and significantly more ended with an HbA1c <7% (49% and 59% vs 33%, respectively; p<0.001). In one add-on study to metformin and a sulfonylurea, Trulicity® 0.75mg and 1.5mg were compared to insulin glargine. The reductions in HbA1c were -0.8% and -1.1% vs -0.6%, respectively, while the changes in body weight were -1.3kg and -1.9kg vs +1.4kg. Nevertheless, in one add-on study with insulin lispro, reductions in HbA1c with Trulicity® 0.75mg and 1.5mg vs insulin glargine were -1.6% and -1.6% vs -1.4%, respectively. The changes in body weight were +0.2kg and -0.9kg vs +2.3kg.

A placebo-controlled and active, open-label comparator (exenatide 10mcg BID) study was performed as an add-on to metformin and a thiazolidinedione (TZD). Placebo and both doses of Trulicity® were double-blind treatments while exenatide was open-label. Results suggested that Trulicity® 0.75mg and 1.5mg use demonstrated statistically significant reductions in HbA1c as compared to placebo and as compared to exenatide (-1.3% and -1.5% vs -0.5% and vs -1.0%; p<0.001 compared to placebo and exenatide). Statistically significantly more taking Trulicity® 0.75mg (66%) and 1.5mg (78%) achieved HbA1c<7% as compared with placebo (43%; p<0.001) and as compared with exenatide (52%; p<0.001). The mean change in body weight was +0.2kg with Trulicity® 0.75mg and -1.3kg with the 1.5mg dose vs +1.2kg with placebo and -1.1kg with exenatide.

In a 2014 phase 3, open-label study by Dungan et al[2], patients inadequately controlled on metformin (N=599) were randomized to receive dulaglutide 1.5mg QW or liraglutide 1.8mg QD, with the primary outcome being non-inferiority of dulaglutide vs liraglutide for the change in HbA1c at 26 weeks. Both treatments significantly reduced HbA1c from baseline. The least-squares (LS) mean reduction in HbA1c was -1.42% with dulaglutide vs -1.36% with liraglutide. This suggested that the reduction in HbA1c with dulaglutide was non-inferior but not superior to that of liraglutide, with a between-treatment difference in HbA1c reduction of -0.06%.

There was no evidence found that supported that Trulicity® was safer or more effective than other preferred treatments for diabetes. It is recommended that Trulicity® remain non-preferred and require prior authorization and be available to the few who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Trulicity [package insert]. Indianapolis, IN: Eli Lilly & Co; 2014.

[2] Dungan KM, Povedano ST, Forst T, et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomized, open-label, phase 3, non-inferiority trial. *Lancet*. 2014. [Epub ahead of print].