# Dulaglutide (Trulicity®)

## Classification

Antidiabetic Agent

## Pharmacology

Dulaglutide is a human GLP-1 receptor agonist (incretin mimetic) with 90% amino acid sequence homology to endogenous human GLP-1. Dulaglutide activates the GLP-1 receptor in pancreatic beta cells leading to glucose-dependent insulin release. It also decreases glucagon secretion, slows gastric emptying, and promotes satiety.

## Indication

- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- Reduce the risk of major adverse cardiovascular events (MACE) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors

## Black Box Warning

Risk of Thyroid C-Cell Tumors

In male and female rats, dulaglutide causes a dose-related and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure. It is unknown whether Trulicity causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans.

Trulicity is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC with use of Trulicity and inform them of symptoms of thyroid tumors (e.g., mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Trulicity.

# Pharmacokinetics

| Pharmacokinetic Parameter | Details |
|---|---|
| Absorption | Tmax = 24-72 h. Site of SC admin (abdomen, upper arm, thigh) had no significant effect on exposure to dulaglutide |
| Distribution | Mean central = 3.09 L, mean peripheral = 5.98 L |
| Metabolism | Endogenously metabolized by dipeptidyl peptidase IV (DPP-IV) and endogenous endopeptidases. Metabolism occurs more slowly compared to endogenous GLP-1 |
| Excretion | Half life = 5 days |

# Dosage/Administration

Recommended starting dose is 0.75 mg SC once weekly. Increase to 1.5 mg once weekly for additional glycemic control. If additional glycemic control is needed after at least 4 weeks on the 1.5 mg dose, increase to 3 mg once weekly. If additional glycemic control is needed after at least 4 weeks on the 3 mg dose, increase to the max dose of 4.5 mg once weekly.

- Administer once weekly, any time of day, with or without food
- Inject SC in the abdomen, thigh, or upper arm
- Rotate injection sites with each dose
- Inspect before use. Should be clear and colorless. Do not use if particulate matter or coloration is seen
- When using with insulin, administer as separate injections and never mix. Both can be injected in the same body region, but not adjacent to each other

# Use in Special Population

## Pregnancy

Risk Summary

Limited data with TRULICITY in pregnant women are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. There are clinical considerations regarding the risks of poorly controlled diabetes in pregnancy. Based on animal reproduction studies, there may be risks to the fetus from exposure to dulaglutide during pregnancy. TRULICITY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In pregnant rats administered dulaglutide during organogenesis, early embryonic deaths, fetal growth reductions, and fetal abnormalities occurred at systemic exposures at least 6-times human exposure at the maximum recommended human dose (MRHD) of 4.5 mg/week. In pregnant rabbits administered dulaglutide during organogenesis, major fetal abnormalities occurred at 5-times human exposure at the MRHD. Adverse embryo/fetal effects in animals occurred in association with decreased maternal weight and food consumption attributed to the pharmacology of dulaglutide.

The estimated background risk of major birth defects is 6–10% in women with pre-gestational diabetes with an HbA1c >7% and has been reported to be as high as 20– 25% in women with an HbA1c >10%. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Clinical Considerations

*Disease-associated maternal and/or embryo/fetal risk*

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia-related morbidity.

## Lactation

Risk Summary

There are no data on the presence of dulaglutide in human milk, the effects on the breastfed infant, or the effects on milk production. The presence of dulaglutide in milk of treated lactating animals was not determined. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRULICITY and any potential adverse effects on the breastfed infant from TRULICITY or from the underlying maternal condition.

## Pediatric Use

Safety and effectiveness of Trulicity have not been established in pediatric patients. Trulicity is not recommended for use in pediatric patients < 18 years.

## Geriatric Use

In the glycemic control trials, 620 (18.6%) TRULICITY-treated patients were 65 years of age or older and 65 (1.9%) TRULICITY-treated patients were 75 years of age or older at baseline. In the TRULICITY 1.5 mg treatment arm of the REWIND

trial, a total of 2619 (52.9%) patients were 65 years of age or older, and 484 (9.8%) patients were 75 years of age or older at baseline.

No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

### Renal Impairment

TRULICITY has been studied in patients with varying degrees of renal function, including a dedicated study in patients with moderate to severe chronic kidney disease. No overall differences in safety or effectiveness were observed in these studies according to renal function.

In a clinical pharmacology study in subjects with renal impairment, including end-stage renal disease (ESRD), no clinically relevant change in dulaglutide pharmacokinetics (PK) was observed. In the 52-week study in patients with type 2 diabetes and moderate to severe renal impairment, the PK behavior of TRULICITY 0.75 mg and 1.5 mg once weekly was similar to that demonstrated in previous clinical studies.

No dose adjustment is recommended in patients with renal impairment including end-stage renal disease (ESRD). Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. Use TRULICITY with caution in patients with ESRD.

### Hepatic Impairment

In a clinical pharmacology study in subjects with varying degrees of hepatic impairment, no clinically relevant change in dulaglutide PK was observed. However, there is limited clinical experience in patients with mild, moderate, or severe hepatic impairment; therefore, use TRULICITY with caution in these patient populations.

### Gastroparesis

Dulaglutide slows gastric emptying. TRULICITY has not been studied in patients with preexisting gastroparesis. Use TRULICITY with caution in patients with gastroparesis.

## Contraindication

Personal or family history of medullary thyroid carcinoma (MTC) or patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)

Prior serious hypersensitivity reaction to dulaglutide or to any of the product components. Serious hypersensitivity reactions including anaphylactic reactions and angioedema have been reported.

# Precautions

## Risk of Thyroid C-cell Tumors

In male and female rats, dulaglutide causes a dose-related and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure. Glucagon-like peptide-1 (GLP-1) receptor agonists have induced thyroid C-cell adenomas and carcinomas in mice and rats at clinically relevant exposures. It is unknown whether TRULICITY will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of dulaglutide-induced rodent thyroid C-cell tumors has not been determined.

One case of MTC was reported in a patient treated with TRULICITY in a clinical study. This patient had pretreatment calcitonin levels approximately 8 times the upper limit of normal (ULN). An additional case of C-cell hyperplasia with elevated calcitonin levels following treatment was reported in the cardiovascular outcomes trial (REWIND). Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

TRULICITY is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of TRULICITY and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with TRULICITY. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin values may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

## Pancreatitis

In a pooled analysis from the original registration studies, 12 (3.4 cases per 1000 patient years) pancreatitis-related adverse reactions were reported in patients exposed to TRULICITY versus 3 in non-incretin comparators (2.7 cases per 1000 patient years). An analysis of adjudicated events revealed 5 cases of confirmed pancreatitis in patients exposed to TRULICITY (1.4 cases per 1000 patient years) versus 1 case in non-incretin comparators (0.88 cases per 1000 patient years).

Based on an analysis of adjudicated events in a clinical study evaluating Trulicity 1.5 mg, 3 mg, or 4.5 mg once weekly, pancreatitis occurred in 1 patient exposed to TRULICITY 1.5 mg (0.2%), in 2 patients exposed to TRULICITY 3 mg (0.3%), and 3 patients exposed to TRULICITY 4.5 mg (0.5%).

After initiation of TRULICITY, observe patients carefully for signs and symptoms of pancreatitis, including persistent severe abdominal pain, sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, promptly discontinue TRULICITY. If pancreatitis is confirmed, TRULICITY should not be restarted. TRULICITY has not been evaluated in patients with a prior history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

## Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin

Patients receiving TRULICITY in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia.

The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.

## Hypersensitivity Reactions

There have been postmarketing reports of serious hypersensitivity reactions including anaphylactic reactions and angioedema in patients treated with TRULICITY. If a hypersensitivity reaction occurs, discontinue TRULICITY; treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity reaction to TRULICITY.

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema or anaphylaxis with

another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to anaphylaxis with TRULICITY.

### Acute Kidney Injury

In patients treated with GLP-1 receptor agonists, including TRULICITY, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events were reported in patients without known underlying renal disease. A majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Because these reactions may worsen renal function, use caution when initiating or escalating doses of TRULICITY in patients with renal impairment. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions.

### Severe Gastrointestinal Disease

Use of Trulicity may be associated with gastrointestinal adverse reactions, sometimes severe. Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

### Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy

In a cardiovascular outcomes trial with a median follow up of 5.4 years involving patients with type 2 diabetes with established cardiovascular disease or multiple cardiovascular risk factors, diabetic retinopathy complications occurred in patients treated with TRULICITY 1.5 mg (1.9%) and placebo (1.5%). These events were prospectively ascertained as a secondary composite endpoint. The proportion of patients with diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (TRULICITY 8.5%, placebo 6.2%) than among patients without a known history of diabetic retinopathy (TRULICITY 1%, placebo 1%).

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

## Adverse Effects

In clinical trials (up to 36 weeks) in patients on dulaglutide 1.5 mg to 4.5 mg, the most common adverse reactions were nausea (13.4-16.4%), diarrhea (7.0-11.4%), vomiting (5.6-9.3%), and dyspepsia (2.8-5.0%).

## Incidence (%) of Hypoglycemia in Placebo-Controlled Trials

| **Add-on to Metformin, 26 wk** | **Placebo** | **Trulicity 0.75 mg** | **Trulicity 1.5 mg** |
|---|---|---|---|
| Number of patients | N = 177 | N = 302 | N = 304 |
| Hypoglycemia w/ glucose level < 54 mg/dL | 0 | 0.3 | 0.7 |

| **Add-on to Metformin + Pioglitazone, 26 wk** | **Placebo** | **Trulicity 0.75 mg** | **Trulicity 1.5 mg** |
|---|---|---|---|
| Number of patients | N = 141 | N = 280 | N = 279 |
| Hypoglycemia with a glucose level < 54 mg/dL | 1.4 | 2.1 | 0 |

| **Add-on to Glimepiride, 24 wk** | **Placebo** | **Trulicity 0.75 mg** | **Trulicity 1.5 mg** |
|---|---|---|---|
| Number of patients | N = 60 | n/a | N = 239 |
| Hypoglycemia with a glucose level < 54 mg/dL | 0 | n/a | 3.3 |

| **In Combin. With Insulin Glargine ±Metformin, 28 wk** | **Placebo** | **Trulicity 0.75 mg** | **Trulicity 1.5 mg** |
|---|---|---|---|
| Number of patients | N = 150 | n/a | N = 150 |
| Hypoglycemia with a glucose level < 54 mg/dL | 9.3 | n/a | 14.7 |

| **Add-on to SGLT2i ± Metformin, 24 wk** | **Placebo** | **Trulicity 0.75 mg** | **Trulicity 1.5 mg** |
|---|---|---|---|
| Number of patients | N = 140 | N = 141 | N = 142 |
| Hypoglycemia with a glucose level < 54 mg/dL | 0.7 | 0.7 | 0.7 |

# Monitoring

Plasma glucose; HbA1c; renal function (in patients reporting severe GI reactions); signs/symptoms of pancreatitis; worsening diabetic retinopathy (in patients with a prior history).

# Interactions

Oral Medications

TRULICITY delays gastric emptying and thus has the potential to reduce the rate of absorption of concomitantly administered oral medications. The delay in gastric emptying is dose-dependent but is attenuated with the recommended dose escalation to higher doses of TRULICITY. The delay is largest after the first dose and diminishes with subsequent doses. In clinical pharmacology studies, TRULICITY 1.5 mg did not affect the absorption of the tested orally administered medications to a clinically relevant degree. There is limited experience with the use of concomitant medications in clinical trials with TRULICITY doses of 3 mg and 4.5 mg.

Monitor drug levels of oral medications with a narrow therapeutic index (e.g., warfarin) when concomitantly administered with TRULICITY.

Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin

When initiating TRULICITY, consider reducing the dose of concomitantly administered insulin secretagogues (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia.

# Efficacy

*Rewind*

REWIND was a multicenter, randomized, double-blind, placebo-controlled trial performed at 371 sites in 24 countries. Men and women ($\geq$ 50 years) with established or newly diagnosed diabetes (HbA1c $\leq$ 9.5%, no lower limit) on stable doses of up to two diabetes meds with or without basal insulin could participate if BMI $\geq$ 23 kg/m2. Patients $\geq$ 50 yo were required to have vascular disease (previous mi, ischemic stroke, revascularization, hospitalization for unstable angina, imaging evidence of myocardial ischemia). Patients $\geq$ 55 yo were required to have myocardial ischemia; coronary, carotid, or lower extremity artery stenosis exceeding 50%; left ventricular hypertrophy; estimated gfr < 60 ml/min; or albuminuria. Patients $\geq$ 60 yo had to have at least two of tobacco use, dyslipidemia, hypertension, or abdominal obesity. Exclusion criteria included eGFR < 15 ml/min, cancer in the previous five years, severe hypoglycemia in the

previous year, life expectancy < 1 year, coronary or cerebrovascular event within the previous 2 months, plans for revascularization.

9901 individuals were randomly assigned to treatment group (dulaglutide, n = 4949; placebo, n = 4952). Mean age was 66.2 years (SD 6.5) and 46.3% were female. 31.5% of participants had previous cardiovascular disease and 22.2% had a baseline eGFR < 60 ml/min. The median duration of diabetes was 9.5 years (IQR 5.5-14.5) and the median HBA1c was 7.2% (IQR 6.6-8.1). Median eGFR was 74.9 ml/min.

Median follow-up was 5.4 years (IQR 5.1-5.9). Current guidelines were used to manage blood pressure, lipids, and other cardiovascular risk factors. Investigators were free to add any glucose-lowering drug apart from another glp-1 receptor agonist or pramlintide.

The primary outcome was the first occurrence of any component of the composite outcome (non-fatal myocardial infarction, non-fatal stroke, and death from cardiovascular causes or unknown causes). The primary outcome occurred in 12.0% of participants taking dulaglutide versus 13.4% of participants taking placebo (HR 0.88, 95% CI 0.79-0.99, p = 0.026). Across the three components of the primary outcome, greatest treatment benefit was seen in the number of non-fatal strokes (HR 0.76, 95% CI 0.61-0.95, p = 0.017). Subgroup analysis showed that hazard ratios were similar for participants with and without previous cardiovascular disease, individuals with HbA1c < 7.2% or $\geq$ 7.2% and in individuals analyzed by age, sex, duration of diabetes, and BMI.

One of the secondary outcomes was a composite microvascular outcome comprised of eye (diabetic retinopathy) or renal outcomes. Renal outcomes included development of urinary albumin-to-creatinine ratio > 300 mg/g, sustained $\geq$ 30% decline in eGFR (based on 2 consecutive eGFR concentrations), chronic renal replacement therapy. The incidence of the composite microvascular outcome was lower in patients taking dulaglutide than in those taking placebo (HR 0.87, 95% CI 0.79-0.95). The difference was driven by the occurrence of fewer composite renal outcomes in the dulaglutide versus the placebo group (HR 0.85, 95% CI 0.77-0.93). Dulaglutide did not significantly affect the incidence of all-cause mortality, heart failure, revascularization, hospital admission for unstable angina.

Compared with patients in the placebo group, patients taking dulaglutide had a 0.61% (95% CI 0.58-0.65) lower HbA1c (p < 0.0001), 1.46 kg (1.25-1.67) lower bodyweight (p < 0.0001), and a 1.70 mm Hg (1.33-2.07) lower systolic blood pressure (p < 0.0001).

Dulaglutide was well tolerated; serious adverse events did not differ significantly between groups. However, 47.4% of participants assigned to dulaglutide reported a gastrointestinal adverse event compared with 34.1% of participants assigned to placebo ($p < 0.0001$). 9.1% of participants taking dulaglutide and 6.3% of participants taking placebo stopped study drug because of an adverse event.

*SUSTAIN 7*

Weekly semaglutide (Ozempic) was compared to weekly dulaglutide (Trulicity) in an open-label, phase 3b, multi-center trial conducted in 1,201 adults with inadequately controlled type 2 diabetes (HbA1c 7.0-10.5%). Patients had been on at least 1500 mg per day of metformin monotherapy for 90 days before screening and were randomized to 40 weeks of SQ once a week treatment with low doses (semaglutide 0.5 mg vs dulaglutide 0.75 mg) and high doses (semaglutide 1.0 mg vs dulaglutide 1.5 mg.). Key exclusion criteria included history of pancreatitis, heart failure (New York Heart Association Class IV), CKD stage 3 and higher, proliferative retinopathy or maculopathy requiring acute treatment.

The primary endpoint was mean percentage HBA1c reduction from baseline to week 40. Mean HBA1c was reduced 1.5 (SE 0.06) percentage points with semaglutide 0.5 mg versus 1.1 (0.05) percentage points with dulaglutide 0.75 mg. At the higher doses, mean HBA1c was reduced 1.8 (SE 0.06) percentage points with semaglutide 1.0 mg versus 1.4 (SE 0.06) percentage points with dulaglutide 1.5 mg. Both estimated treatment differences were statistically significant ($p < 0.0001$)

The secondary endpoint was change from baseline to week 40 in bodyweight. At week 40, mean body weight was reduced by 4.6 kg (SE 0.28) with semaglutide 0.5 mg versus 2.3 kg (0.27) with dulaglutide 0.75 mg (treatment difference -2.26 (95% CI -3.02 to – 1.51, $p < 0.001$. At the higher doses, mean body weight was reduced by 6.5 kg (0.28) with semaglutide 1.0 mg versus 3.0 kg (0.27) with dulaglutide 1.5 mg (-3.55 kg [-4.32 to -2.78]; $p < 0.0001$).

GI disorders were the most frequently reported adverse event, occurring in 43% of patients receiving semaglutide 0.5 mg, 44% of patients receiving semaglutide 1.0 mg, 33% of patients receiving dulaglutide 0.75 mg and 48% of patients receiving dulaglutide 1.5 mg. Most of the adverse events that led to premature treatment discontinuation were gastrointestinal side effects that occurred early in the trial. Rates of treatment discontinuation were 8% in the semaglutide 0.5 mg group, 10% in the semaglutide 1.0 mg group, 5% in the dulaglutide 0.75 mg group, and 7% in the dulaglutide 1.5 mg group.

# Dosage Forms/Cost

Single-dose pen (includes needles): 0.75 mg/0.5 ml, 1.5 mg/0.5 ml, 3 mg/0.5 ml, 4.5 mg/0.5 ml:

Per GoodRx, month supply of each strength is $771.44

# Special Considerations

**SH, SSLC GLP-1 agonist purchases 9/1/21-2/28/22**

| Medication purchased | Units Purchased |
|---|---|
| Byetta (exenatide) | 11 |
| Bydureon (exenatide extended-release) | 4 |
| Victoza (liraglutide) prefilled pen | 105 |
| Saxenda (liraglutide) prefilled pen | 30 |
| Trulicity pen (dulaglutide) | 300 |
| Ozempic (semaglutide) | 13 |
| Wegovy (semaglutide) | 6 |
| Rybelsus (semaglutide) tablets | 390 |

# Summary/Conclusion

In 2019, liraglutide (Victoza) was the first glp-1 agonist added to the formulary. Liraglutide was chosen because, at the time, it was the most widely used glp-1 receptor agonist in the state system and the only glp-1 agonist approved to reduce CV risk in patients with established CV disease. It had also shown efficacy in the treatment of metabolic disturbances in patients treated with antipsychotics.

In 2020, semaglutide sc (Ozempic) and dulaglutide (Trulicity) were both approved to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes. Semaglutide sc (Ozempic) is approved to reduce MACE in adults with type 2 diabetes and established cardiovascular disease; dulaglutide (Trulicity) is approved to reduce MACE in adults with type 2 diabetes who have established cardiovascular

disease or multiple cardiovascular risk factors. For the composite outcome of cv death, nonfatal MI, and nonfatal stroke, oral semaglutide (Rybelsus) demonstrated non-inferiority to placebo in a pre-approval trial designed to rule out an unacceptable increase in CV risk. The cv effects of oral semaglutide will be further tested in a large, longer term outcomes trial.

Per ADA 2022, glucagon-like peptide 1 receptor agonists with proven CVD benefit ( with or without metformin) are appropriate initial therapy for individuals with type 2 diabetes with or at high risk for ASCVD. Along with SGLT2i with proven CVD benefit, GLP-1 RA's are also an appropriate first line choice for CV risk reduction in diabetic patients with CKD without albuminuria. GLP-1 RA's have improved secondary renal end points in CVOTs but their effects on hard renal outcomes are not as well established as those of the SGLT2i. They are listed as an alternative therapy for diabetic patients with CKD and albuminuria ($\geq$ 200 mg/g creatinine) if SGLT2i are not tolerated or contraindicated. If injectable therapy is needed to reduce A1c, ADA 2022 also recommends GLP-1 RA over insulin, when possible.

# Recommendation

Dulaglutide (Trulicity) should be added to the formulary.

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