With the addition of the CV indication, Trulicity® is proven to do more[1]

Trulicity (dulaglutide) is indicated

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use: Has not been studied in patients with a history of pancreatitis; consider another antidiabetic therapy. Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. Not a substitute for insulin. Has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. Not for patients with pre-existing severe gastrointestinal disease.

Select Important Safety Information

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 as human relevance of dulaglutide-induced rodent thyroid C-cell tumors has not been determined.

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 (eg, 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.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

CV=cardiovascular

once weekly
trulicity® (dulaglutide) injection
0.75 mg/0.5 mL, 1.5 mg/0.5 mL

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Frustrated that her current therapy isn't enough

- A1C 8%-10% and CV risk factors
- Anxious about what's next[2,3]

The more the next medication requires her to do, the less likely she may be to take it[4,5]

She needs motivation now

Hypothetical scenario

Select Important Safety Information

- Trulicity is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2, and in patients with a prior serious hypersensitivity reaction to dulaglutide or to any of the product components.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

Trulicity offers powerful A1C reduction*

*In clinical studies, the range of A1C reduction from baseline was 0.7% to 1.6% for the 0.75 mg dose and 0.8% to 1.6% for the 1.5 mg dose.[1,6]
Mean A1C reduction for Victoza 1.8 mg at week 26 (primary endpoint) was 1.4%.

Patients saw a 1.4% A1C reduction* with Trulicity 1.5 mg as the only add-on to metformin[6]

In a subset analysis by baseline A1C, Trulicity showed A1C reduction in both subsets[7]

Baseline A1C ≤8.5%
(n=219)

-1.2%

from **7.7%** to **6.5%**

Victoza results: Mean A1C (%) for Victoza 1.8 mg (n=218) in patients with a baseline A1C ≤8.5% at baseline: 7.7; week 26: 6.5.

Baseline A1C >8.5%
(n=80)

-2.1%

from **9.1%** to **7.0%**

Victoza results: Mean A1C (%) for Victoza 1.8 mg (n=82) in patients with a baseline A1C >8.5% at baseline: 9.1; week 26: 7.1.

Data represent least-squares mean.

- The data presented are not intended to make clinical comparisons between any subsets within or across products at any time point
- Patients were stratified by baseline A1C % (≤8.5, >8.5) during randomization
- No significant treatment by baseline A1C by visit interaction was observed

Select Important Safety Information

- Pancreatitis has been reported in clinical trials. Observe patients for signs and symptoms including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue Trulicity promptly. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

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once weekly
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Recommended starting dose is 0.75 mg. Dose can be increased to 1.5 mg for additional A1C reduction.

Study Description[6]

- Victoza® 1.8 mg QD, SC (n=300; mean baseline A1C: 8.1%); Trulicity 1.5 mg QW, SC (n=299; mean baseline A1C: 8.1%)
- 26-week, randomized, open-label comparator phase 3b study of adult patients with type 2 diabetes treated with metformin ≥1500 mg/day
- Primary objective was to demonstrate noninferiority of Trulicity 1.5 mg vs Victoza 1.8 mg on A1C change from baseline at 26 weeks (-1.42% vs -1.36%, respectively; difference of -0.06%; 95% CI [-0.19, 0.07]; 2-sided alpha level of 0.05 for noninferiority with 0.4% margin; mixed-model repeated measures analysis)
- Primary objective of noninferiority for A1C reduction was met; secondary endpoint of superiority was not met

Select Important Safety Information

- Cases of medullary thyroid carcinoma (MTC) in patients treated with liraglutide, another GLP-1 RA, 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 RA use in humans. If serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging, the patient should be further evaluated.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

Reduction in fasting and postprandial glucose at 48 hours after first dose of Trulicity[1,8-10]

These data are from a pharmacodynamics study.

Study Description

- 6-week, multicenter, parallel-design, double-blind, part-randomized, placebo-controlled, multiple-dose, phase 1 study in patients ≥65 years old with type 2 diabetes treated with oral antihyperglycemic medications except sulfonylureas, disaccharidase inhibitors, and meglitinides
- Study arms included placebo (n=8); Trulicity 0.5 mg (n=9), not a marketed dose; Trulicity 0.75 mg (n=11); and Trulicity 1.5 mg (n=9)
- Primary objective was to evaluate the safety and tolerability of Trulicity 0.5 mg, 0.75 mg, and 1.5 mg for 6 weeks; mixed effect linear model; primary objective met
- Data presented are LS mean change from baseline and are secondary endpoints

FSG=fasting serum glucose

PPG=postprandial serum glucose

Select Important Safety Information

- The risk of hypoglycemia is increased when Trulicity is used in combination with insulin secretagogues (eg, sulfonylureas) or insulin. Patients may require a lower dose of sulfonylurea or insulin to reduce the risk of hypoglycemia.

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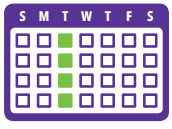
In addition to glycemic control, could the Trulicity experience give your patients the motivation they need to start and stay on a new treatment?*[1,2,11-14]



Once weekly

Pen that patients preferred†

Possible weight loss‡

*In a study, 97% of injection-naïve patients were willing to continue using the Trulicity Pen. The primary objective of a success rate significantly greater than 80% at the fourth weekly injection was met. 99.1% [95% CI: 96.6% to 99.7%] (n=209) of patients successfully completed each step in the sequence of drug administration after proper self-injection training at baseline. Limitations include the administration of placebo rather than active drug product. After the final self-injection, patients completed an 8-item experience module (secondary endpoint). 203 (96.7%) out of 210 patients reported that they were "mostly willing" or "definitely willing" to continue using the single-dose pen.[14]

†More than six times as many patients preferred the Trulicity Pen over the Ozempic pen (84% vs 12%; $P<.0001$).[15]

These data make no representation or conclusion as to the factors contributing to patient preference.

These data do not establish clinical comparability of the products for any indications and should not be seen as making any claim regarding efficacy and safety.

Study Description[15]

- Open-label, multicenter, randomized, crossover study to evaluate patient preference between the Trulicity Pen and the Ozempic pen among adults with type 2 diabetes who were naïve to self-injecting and injecting others (N=310)
- Patients read and were trained on the Instructions for Use for each device containing the lowest available dose of medication prior to administering mock injections into an injection pad. After using both devices, patients reported which device they preferred (primary endpoint) and completed a 10-item preference questionnaire. Patients completed questions on willingness to use before device trainings and after using the devices
- Primary outcome: Difference in preference between two devices measured by global preference item “Overall which device do you prefer?”
- Limitations include the use of injection pads rather than actual injections and the participants only used each device one time

‡Trulicity is not indicated for weight loss.

In clinical studies, weight change was a secondary endpoint. Mean weight change was -1.1 lb to -6.8 lb at the 1.5 mg dose and +0.4 lb to -6.0 lb at the 0.75 mg dose.[1,6]

Select Important Safety Information

- There have been postmarketing reports of serious hypersensitivity reactions (eg, anaphylactic reactions and angioedema) in patients treated with Trulicity. Instruct patients who experience symptoms to discontinue Trulicity and promptly seek medical advice. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 RA because it is unknown whether they will be predisposed to anaphylaxis with Trulicity.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

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With the addition of the CV indication, Trulicity is proven to do more[1]

Trulicity is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke) in adults with type 2 diabetes mellitus[1]

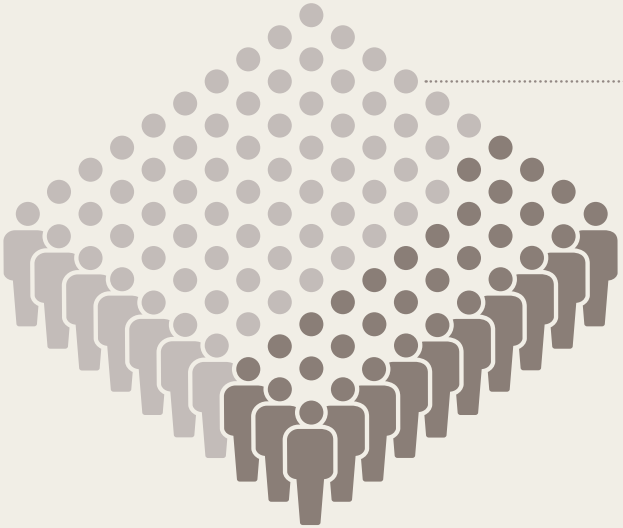
- Without established cardiovascular disease (CVD) who have multiple CV risk factors
- With established CVD

Select Important Safety Information

- There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, sometimes requiring hemodialysis, in patients treated with GLP-1 receptor agonists. A majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. In patients with renal impairment, use caution when initiating or escalating doses of Trulicity and monitor renal function in patients experiencing severe adverse gastrointestinal reactions.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

People with type 2 diabetes are at CV risk
Not all have CVD[16]



No CVD*
68%

CVD*
32%

*68% data was calculated and assumes both patients with known CVD and unevaluated or unknown CVD status.

- Data for adult patients with type 2 diabetes with established CVD is from a systematic literature review of global scientific evidence in a 2018 issue of the journal *Cardiovascular Diabetology* which analyzed 57 studies from 25 countries, including the US. This review included prevalence studies, cross-sectional surveys, incidence studies that included population-based baseline and follow-up data, peer-reviewed studies, published articles, and abstracts from scientific meetings
- Data were analyzed descriptively, with sums, averages, medians, and ranges reported. Prevalence was weighted by inverse variance. The prevalence of any cardiovascular disease was 32.2% (95% confidence interval 30.0-34.4%). Some articles focused on a single outcome, whereas others focused on several outcomes. As a result, the calculated prevalence rates may represent underestimates, as not all studies reported all outcomes
- Limitations of this review include varying descriptions of CVD and its associated conditions, as well as the types of studies included. Excluded from the consideration of CVD were peripheral artery disease, rheumatic heart disease, cardiac dysrhythmias, or requirement for surgery

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

A GLP-1 RA CVOT designed differently than any other[17-24]

REWIND is the only GLP-1 RA CVOT to include a majority of patients without established CVD*

	Trulicity® REWIND[17,18]	Bydureon® EXSCEL[19]	Victoza® LEADER[20]	Ozempic® SUSTAIN-6[21]	Rybelsus® PIONEER 6[22,23]	Adlyxin® ELIXA[24]
Number of patients	9901	14752	9340	3297	3183	6068
Prior CVD,† %	31	73	81	83	85	100
Female, %	46	38	36	39	32	31
Median follow-up	5.4 years	3.2 years	3.8 years	2.1 years	1.3 years	2.1 years

*In REWIND, patients without established CV disease had multiple CV risk factors.

†Criteria for prior CVD may vary between study protocols. Please refer to study descriptions on next page for individual study criteria.

No comparison can be made between GLP-1 RA CVOT outcomes due to differences in study design, population, and key inclusion/exclusion criteria.

CVOT=cardiovascular outcomes trial

For full study descriptions, see page 11.

Select Important Safety Information

- Use of Trulicity may be associated with gastrointestinal adverse reactions, sometimes severe. Trulicity has not been studied in and is not recommended for patients with a history of severe gastrointestinal disease (eg, severe gastroparesis).

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Indications and Limitations of Use

Trulicity

Indication[1]: Trulicity is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use[1]

- Has not been studied in patients with a history of pancreatitis. Consider another antidiabetic therapy.
- Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. Not a substitute for insulin.
- Has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. Not for patients with pre-existing severe gastrointestinal disease.

Rybelsus

Indication[26]: Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use[26]

- Rybelsus is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans.
- Rybelsus has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Rybelsus is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

Ozempic

Indication[27]: Ozempic is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use[27]

- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic is not a substitute for insulin. Ozempic is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

Victoza

Indication[28]: Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus,
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use[28]

- Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Victoza and prandial insulin has not been studied.

Bydureon

Indication[29]: Bydureon is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use[29]

- Bydureon is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon is not a substitute for insulin. Bydureon is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Bydureon with prandial insulin has not been studied.
- Bydureon is an extended-release formulation of exenatide. Bydureon should not be used with other products containing the active ingredient exenatide.
- Bydureon has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Select Important Safety Information

- Diabetic retinopathy complications have been reported in a cardiovascular outcomes trial. Monitor patients with a history of diabetic retinopathy.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

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Study Descriptions

REWIND[17,18]

- Multicenter, randomized, double-blind, placebo-controlled, event-driven trial designed to assess whether once-weekly Trulicity 1.5 mg safely reduces the incidence of CV outcomes compared to placebo in adult patients with type 2 diabetes with and without CVD
- Key inclusion criteria: Established or newly detected type 2 diabetes with an A1C ≤9.5%; stable dose of up to 2 oral glucose-lowering drugs with or without basal insulin; BMI ≥23 kg/m^2; age ≥50 years with established clinical vascular disease,* OR age ≥55 years and subclinical† vascular disease, OR age ≥60 years and at least 2 or more CV risk factors‡
- Key exclusion criteria: Uncontrolled diabetes; severe hypoglycemia in preceding year; coronary or cerebrovascular event in preceding 2 months; plans to revascularize; estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2; on dialysis; gastric bypass or emptying abnormality; prior pancreatitis; liver disease; family or personal history of C-cell hyperplasia, medullary thyroid cancer, multiple endocrine neoplasia (MEN) 2A or 2B, or calcitonin ≥20 pg/mL; unwilling to stop GLP-1 RA, dipeptidyl peptidase-4 (DPP-4) inhibitor, or weight loss drug; cancer within preceding 5 years; possible pregnancy; life expectancy <1 year
- 9901 patients were randomized to receive Trulicity 1.5 mg or same volume of placebo in addition to standard of care treatments such as oral antidiabetic treatments, insulin, and antihypertensive, antiplatelet, and lipid-lowering therapies; patients were assessed every 6 months until 1200 confirmed primary outcomes had accrued
- Primary outcome was the first occurrence of the composite of either nonfatal myocardial infarction (MI), nonfatal stroke, or CV death (MACE-3). All outcomes occurring on or after randomization were included in analysis; Kaplan-Meier estimates were used to generate cumulative risks and Cox proportional hazard models were used to determine the effect of intervention on the outcome and to estimate HR and 95% CIs

*History of MI, ischemic stroke, revascularization, hospitalization for unstable angina with concordant new ischemic electrocardiogram changes, or a positive stress test with concordant imaging.[18]

†Myocardial ischemia, coronary, carotid, or lower extremity artery stenosis exceeding 50%, ankle to brachial index <0.9, hypertension with left ventricular hypertrophy, eGFR <60 mL/min per 1.73m^2, or albuminuria.[18]

‡Tobacco use, dyslipidemia, hypertension, or abdominal obesity.[17]

EXSCEL[19]

- Pragmatic, randomized, double-blind, placebo-controlled, parallel-group, event-driven trial to assess the long-term cardiovascular safety and efficacy of Bydureon in patients with type 2 diabetes
- Key inclusion criteria: ≥18 years of age with an A1C ≥6.5% to ≤10.0%; had been treated with ≤3 oral antihyperglycemic agents or insulin, alone or in combination with ≤2 oral antihyperglycemic agents; designed to have approximately 70% of patients with previous cardiovascular events defined as at least one of the following: history of major clinical manifestation of coronary artery disease (myocardial infarction, coronary revascularization, or coronary angiography showing at least one stenosis ≥50%); ischemic cerebrovascular disease (history of ischemic stroke or history of carotid disease with ≥50% stenosis); or atherosclerotic peripheral arterial disease (amputation due to vascular disease, symptoms of intermittent claudication confirmed by an ankle to brachial index or toe to brachial index <0.9, or history of revascularization)
- 14752 patients were randomized to receive either Bydureon 2 mg (QW,SC) or matched placebo, in addition to standard of care
- Primary composite outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, or CV death

LEADER[20]

- Multicenter, randomized, double-blind, placebo-controlled, time- and event-driven trial to assess the long-term effects of Victoza on CV outcomes and other clinically important events in patients with type 2 diabetes
- Key inclusion criteria: Patients with type 2 diabetes with an A1C ≥7.0%, not previously treated with drugs for type 2 diabetes or had been treated with one or more antihyperglycemic agents with or without insulin, ≥50 years of age with at least one CV condition (coronary heart disease, cerebrovascular disease, peripheral vascular disease, chronic kidney disease of stage ≥3, or chronic heart failure [New York Heart Association class II or III]), ≥60 years of age with at least one CV risk factor (microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or an ankle to brachial index <0.9)
- 9340 patients were randomized to receive either Victoza 1.8 mg (or maximum tolerated dose QD, SC) or matched placebo, in addition to standard of care
- Primary composite outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, or CV death

SUSTAIN-6[21]

- Randomized, double-blind, placebo-controlled, parallel-group, event-driven trial to assess the noninferiority of Ozempic as compared to placebo in terms of cardiovascular safety in patients with type 2 diabetes
- Key inclusion criteria: Type 2 diabetes and an A1C ≥7.0%; not previously treated for type 2 diabetes with an antihyperglycemic drug or had been treated with ≤2 oral antihyperglycemic agents with or without basal or premixed insulin; ≥50 years of age with established cardiovascular disease (previous cardiovascular, cerebrovascular, or peripheral vascular disease), chronic heart failure (New York Heart Association class II or III), or chronic kidney disease stage ≥3; ≥60 years of age with at least one CV risk factor (microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or an ankle to brachial index <0.9)
- 3297 patients were randomized to receive either Ozempic 0.5 mg or 1.0 mg (QW, SC) or volume-matched placebo, in addition to standard of care
- Primary composite outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, or CV death

PIONEER 6[22,23]

- Randomized, double-blind, placebo-controlled, event-driven trial to assess the cardiovascular safety of Rybelsus in patients with type 2 diabetes
- Key inclusion criteria: Patients with type 2 diabetes, age ≥50 years with established CVD (prior myocardial infarction; prior stroke or transient ischemic attack; prior coronary, carotid or peripheral arterial revascularization; >50% stenosis of coronary, carotid, or lower extremity arteries; documented history of symptomatic coronary heart disease; documented asymptomatic cardiac ischemia or chronic heart failure [New York Heart Association class II or III]) or moderate (stage 3) chronic kidney disease; age ≥60 years with at least one cardiovascular risk factor (microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or ankle to brachial index <0.9)
- 3183 patients were randomized to receive either Rybelsus (target dose of 14 mg QD, PO) or placebo, in addition to standard of care
- Primary composite outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, or CV death

ELIXA[24]

- Multicenter, randomized, double-blind, placebo-controlled, event-driven trial to assess the effect of Adlyxin on cardiovascular outcomes in patients with type 2 diabetes who had had a recent acute coronary syndrome, defined as an ST-segment elevation myocardial infarction (STEMI), non-STEMI, or unstable angina
- Key inclusion criteria: Patients with type 2 diabetes who had had an acute coronary event ≤180 days prior to screening
- Key exclusion criteria: Age less than 30 years, A1C less than 5.5% or greater than 11%
- 6068 patients were randomized to receive either Adlyxin 10-20ug (QD, SC) or placebo, in addition to standard of care
- Primary composite outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, CV death or hospitalization for unstable angina

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Trulicity is the first and only GLP-1 RA to

Reduce the risk of CV death, nonfatal MI, or nonfatal stroke* in both primary and secondary prevention† patients[1]

*Trulicity 1.5 mg reduced the risk of MACE-3 (CV death, nonfatal MI, or nonfatal stroke) by 12% in patients without established CVD who have multiple CV risk factors and patients with established CVD.[17]

†Primary prevention: Reducing the risk of atherosclerotic cardiovascular disease (ASCVD) by preventing or managing risk factors. Secondary prevention: Reducing the risk of another event in people who have had a serious CV incident or procedure.[25]

CV indications for GLP-1 RAs‡

	Trulicity[1]	Rybelsus[26]	Ozempic[27]	Victoza[28]	Bydureon[29]
Primary prevention patients (multiple CV risk factors)	✓				
Secondary prevention patients (established CVD)	✓		✓	✓	

‡Indicated for risk reduction of major adverse CV events (CV death, nonfatal MI, nonfatal stroke).

This chart includes oral or injectable GLP-1 RAs that are marketed in the US and have a CVOT.

MI=myocardial infarction

MACE=major adverse cardiovascular events

For product indication statements, see page 10.

Select Important Safety Information

- The most common adverse reactions (excluding hypoglycemia) reported in ≥5% of Trulicity-treated patients in placebo-controlled clinical trials (placebo, Trulicity 0.75 mg, and Trulicity 1.5 mg) were nausea (5.3%, 12.4%, 21.1%), diarrhea (6.7%, 8.9%, 12.6%), vomiting (2.3%, 6.0%, 12.7%), abdominal pain (4.9%, 6.5%, 9.4%), decreased appetite (1.6%, 4.9%, 8.6%), dyspepsia (2.3%, 4.1%, 5.8%), and fatigue (2.6%, 4.2%, 5.6%).

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Even with a majority primary prevention patient population,* Trulicity showed a significant reduction of MACE-3†[17]

12%
RISK REDUCTION OF MACE-3†

Trulicity demonstrated a consistent effect on MACE-3 across primary and secondary prevention patients*‡[17]

For patients with prior CVD,§ the primary composite outcome occurred in 280 of 1560 (17.9%) participants assigned to Trulicity and 315 of 1554 (20.3%) participants assigned to placebo (hazard ratio [HR]=0.87), 95% confidence interval [CI]: 0.74-1.02).

For patients without prior CVD, the primary composite outcome occurred in 277 of 3093 (8.9%) participants assigned to Trulicity and 317 of 3128 (10.1%) participants assigned to placebo (HR=0.87 [95% CI: 0.74-1.02]).

The safety profile of Trulicity was consistent with the GLP-1 receptor agonist class.[17] The most common adverse events leading to the discontinuation of Trulicity were gastrointestinal events.[30]

*Primary prevention: Reducing the risk of ASCVD by preventing or managing risk factors. Secondary prevention: Reducing the risk of another event in people who have had a serious CV incident or procedure.

†The primary composite outcome (MACE-3 comprising CV death, nonfatal MI, or nonfatal stroke) occurred in 594 (12.0%) participants assigned to Trulicity + standard of care and 663 (13.4%) participants assigned to placebo + standard of care (HR=0.88, 95% CI: 0.79-0.99; *P*=.026).

‡Subgroup analysis was prespecified, exploratory, and not adjusted for multiple testing. Consistency of treatment effects in subgroups was assessed by including the subgroup and interaction term in the Cox model.

§REWIND defined established (prior) CV disease as including at least one of the following conditions: MI, ischemic stroke, unstable angina, revascularization, hospitalization for ischemia related events, and/or documented myocardial ischemia.

For study description, see page 11.

Select Important Safety Information

- Trulicity slows gastric emptying, which may impact absorption of concomitantly administered oral medications. Use caution when oral medications are administered with Trulicity. Monitor drug levels of oral medications with a narrow therapeutic index when concomitantly administered. In clinical pharmacology studies, Trulicity did not affect the absorption of the tested, orally administered medications to a clinically relevant degree.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

Risk reduction seen even with a relatively well-controlled mean baseline A1C for patients with type 2 diabetes[17,18]

REWIND participants had lower baseline A1C levels compared to other GLP-1 RA CVOTs[18-22,24,31]

Mean Baseline A1C

Trulicity REWIND[18]	Bydureon EXSCEL[19]	Victoza LEADER[20]	Ozempic SUSTAIN-6[21]	Rybelsus PIONEER 6[22]	Adlyxin ELIXA[24,31]
7.3%	8.0 (median)	8.7%	8.7%	8.2%	7.7%

No comparison can be made between GLP-1 RA CVOT outcomes due to differences in study design, population, and key inclusion/exclusion criteria.

Select Important Safety Information

- Limited data with Trulicity in pregnant women are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. Based on animal reproduction studies, there may be risks to the fetus from exposure to dulaglutide. Use only if potential benefit justifies potential risk to fetus.

Please see Important Safety Information regarding Trulicity on page 15 and full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

once weekly
trulicity®
(dulaglutide) injection
0.75 mg/0.5 mL, 1.5 mg/0.5 mL

Important Safety Information

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 as human relevance of dulaglutide-induced rodent thyroid C-cell tumors has not been determined.

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 (eg, 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.

Trulicity is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with a prior serious hypersensitivity reaction to dulaglutide or any of the product components.

Risk of Thyroid C-cell Tumors: Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist (GLP-1 RA), 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 RA use in humans. If serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging, the patient should be further evaluated.

Pancreatitis: Has been reported in clinical trials. Observe patients for signs and symptoms including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue Trulicity promptly. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Hypoglycemia: The risk of hypoglycemia is increased when Trulicity is used in combination with insulin secretagogues (eg, sulfonylureas) or insulin. Patients may require a lower dose of the sulfonylurea or insulin to reduce the risk of hypoglycemia.

Hypersensitivity Reactions: There have been postmarketing reports of serious hypersensitivity reactions (eg, anaphylactic reactions and angioedema) in patients treated with Trulicity. Instruct patients who experience symptoms to discontinue Trulicity and promptly seek medical advice. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist as it is unknown whether they will be predisposed to anaphylaxis with Trulicity.

Acute Kidney Injury: In patients treated with GLP-1 RAs, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure, sometimes requiring hemodialysis. A majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. In patients with renal impairment, use caution when initiating or escalating doses of Trulicity and monitor renal function in patients experiencing 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: Have been reported in a cardiovascular outcomes trial. Monitor patients with a history of diabetic retinopathy.

The most common adverse reactions (excluding hypoglycemia) reported in ≥5% of Trulicity-treated patients in placebo-controlled trials (placebo, Trulicity 0.75 mg, and Trulicity 1.5 mg) were nausea (5.3%, 12.4%, 21.1%), diarrhea (6.7%, 8.9%, 12.6%), vomiting (2.3%, 6.0%, 12.7%), abdominal pain (4.9%, 6.5%, 9.4%), decreased appetite (1.6%, 4.9%, 8.6%), dyspepsia (2.3%, 4.1%, 5.8%), and fatigue (2.6%, 4.2%, 5.6%).

Gastric emptying is slowed by Trulicity, which may impact absorption of concomitantly administered oral medications. Use caution when oral medications are used with Trulicity. Drug levels of oral medications with a narrow therapeutic index should be adequately monitored when concomitantly administered with Trulicity. In clinical pharmacology studies, Trulicity did not affect the absorption of the tested, orally administered medications to a clinically relevant degree.

Pregnancy: Limited data with Trulicity in pregnant women are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. Based on animal reproduction studies, there may be risks to the fetus from exposure to dulaglutide. Use only if potential benefit justifies the potential risk to the fetus.

Lactation: 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 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 and use is not recommended in patients less than 18 years of age.

Please see full Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, Medication Guide and Instructions for Use.

Please see Instructions for Use included with the pen.

DG HCP ISI FEB2020

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0.75 mg/0.5 mL, 1.5 mg/0.5 mL

Study Description[14]

- Phase 3b, multicenter, single-arm, outpatient study on the safe and effective use of the Trulicity single-dose pen in patients with type 2 diabetes who were naïve to self-injection and injecting others (n=214)
- The primary objective of a success rate significantly greater than 80% at the fourth weekly injection was met. 99.1% [95% CI: 96.6% to 99.7%] (n=209) of patients successfully completed each step in the sequence of drug administration after proper self-injection training at baseline
- Limitations include the administration of placebo rather than active drug product and the willingness of injection-naïve patients to self-inject, which may not be entirely representative of an injection-naïve type 2 diabetes patient population. The patients in this study with fairly well-controlled type 2 diabetes may not be entirely representative of an injection-naïve population progressing to injectable therapy. In clinical practice, patient training on self-injection with the single-dose pen may differ from the method in this study
- After the final self-injection, patients completed a 12-item ease of use module (secondary endpoint). 208 (99%) out of 210 patients reported that overall, single dose pen was "easy" or "very easy" to use

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The only GLP-1 RA that provides these three benefits together

Powerful A1C reduction*[1,6]

Simply delivered†[14]

Proven CV benefit in both primary and secondary prevention patients‡§[17]

Recommended starting dose is 0.75 mg. Dose can be increased to 1.5 mg.

*In clinical studies, the range of A1C reduction from baseline was 0.7% to 1.6% for the 0.75 mg dose and 0.8% to 1.6% for the 1.5 mg dose.[1,6]

†In a study, 99% of patients reported that overall, the Trulicity Pen was easy or very easy to use.[14] For study description, see page 19.

‡Trulicity 1.5 mg reduced the risk of MACE-3 (CV death, nonfatal MI, nonfatal stroke) by 12% in patients without established CVD who have multiple CV risk factors and patients with established CVD.[17]

§Primary prevention: Reducing the risk of ASCVD by preventing or managing risk factors. Secondary prevention: Reducing the risk of another event in people who have had a serious CV incident or procedure.[25]

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