TRULICITY (dulaglutide) injection, for subcutaneous use

Initial U.S. Approval: 2014

BOXED WARNING: RISK OF THYROID C-CELL TUMORS

See full prescribing information for complete boxed warning.

- Dulaglutide causes thyroid C-cell tumors in rats. It is unknown whether TRULICITY causes 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 (5.1, 13.1).
- 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 and symptoms of thyroid tumors (4.1, 5.1).

RECENT MAJOR CHANGES

03/2015

INDICATIONS AND USAGE

TRULICITY™ is a glucagon-like peptide (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise (1, 5.1).
- Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with history of pancreatitis (5.2).
- Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis.
- Not for patients with pre-existing severe gastrointestinal disease.
- Has not been studied in combination with basal insulin.

DOSEAGE FORMS AND STRENGTHS

Injection: 1.5 mg/0.5 mL solution in a single-dose prefilled syringe (3)
Injection: 0.75 mg/0.5 mL solution in a single-dose prefilled syringe (3)
Injection: 1.5 mg/0.5 mL solution in a single-dose pen (3)
Injection: 0.75 mg/0.5 mL solution in a single-dose pen (3)

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF THYROID C-CELL TUMORS

1 INDICATIONS AND USAGE
1.1 Limitations of Use

2 DOSAGE AND ADMINISTRATION
2.1 Dosage
2.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin
2.3 Dosage in Patients with Renal Impairment
2.4 Important Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS
4.1 Medullary Thyroid Carcinoma
4.2 Hypersensitivity

5 WARNINGS AND PRECAUTIONS
5.1 Risk of Thyroid C-cell Tumors
5.2 Pancreatitis
5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin
5.4 Hypersensitivity Reactions

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

7 DRUG INTERACTIONS

7.1 Oral Medications

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
8.2 Nursing Mothers
8.3 Kidney Disease
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Hepatic Impairment
8.7 Renal Impairment
8.8 Gastroesophageal Reflux Disease

9 OVERDOSAGE

10 DESCRIPTION

11 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
12.2 Pharmacodynamics

12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

14.1 Monotherapy
14.2 Combination Therapy

15 HOW SUPPLIED/STORAGE AND HANDLING

15.1 How Supplied
15.2 Storage and Handling

16 PATIENT COUNSELING INFORMATION

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

TRULICITY (dulaglutide) injection, for subcutaneous use
TRU-0003-USPI-20150309

TRULICITY (dulaglutide) injection, for subcutaneous use
TRU-0003-USPI-20150309
TRULICITY (dulaglutide) injection, for subcutaneous use

1 INDICATIONS AND USAGE

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

1.1 Limitations of Use

TRULICITY® 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. TRULICITY® is only for patients to whom the potential benefits outweigh the potential risk. [see Warnings and Precautions (5.1)].

TRULICITY® has not been studied in patients with a history of pancreatitis. [see Warnings and Precautions (5.2)]. Consider other anti-diabetic therapies in patients with a history of pancreatitis.

TRULICITY® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. TRULICITY® is not a substitute for insulin.

TRULICITY® has not been studied in patients with severe gastrointestinal disease, including severe malabsorption. The use of TRULICITY® is not recommended in patients with pre-existing severe gastrointestinal disease. [see Warnings and Precautions (5.6)].

The concurrent use of TRULICITY® and basal insulin has not been studied.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

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. The maximum recommended dose is 1.5 mg once weekly.

Administer TRULICITY® once weekly, any time of day, with or without food. TRULICITY® should be injected subcutaneously in the abdomen, thigh, or upper arm.

If a dose is missed, instruct patients to administer as soon as possible if there are at least 3 days (72 hours) until the next scheduled dose. If less than 3 days remain before the next scheduled dose, skip the missed dose and administer the next dose on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

The day of weekly administration can be changed if necessary as long as the last dose was administered 3 or more days before.

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

When initiating TRULICITY®, consider reducing the dosage of concomitantly administered insulin secretagogues (e.g., sulfonylureas) or insulin to reduce the risk of hypoglycemia. [see Warnings and Precautions (5.3)].

2.3 Dosage in Patients with Renal Impairment

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. [see Warnings and Precautions (5.5), Use in Specific Populations (8.7), Clinical Pharmacology (12.5)].

2.4 Important Administration Instructions

Prior to initiation of TRULICITY®, patients should be trained by their healthcare professional on proper injection technique. Training reduces the risk of administration errors such as improper injection site, needle sticks, and incomplete dosing. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations. The instructions can also be found at www.trulicity.com.

When using TRULICITY® with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject TRULICITY® and insulin in the same body region but the injections should not be adjacent to each other.

When injecting in the same body region, advise patients to use a different injection site each week. TRULICITY® should not be administered intravenously or intramuscularly.

TRULICITY® solution should be visually inspected for particulate matter and discoloration prior to administration.

3 DOSAGE FORMS AND STRENGTHS

- Injection: 0.75 mg/mL solution in a single-dose pen
- Injection: 1.5 mg/mL solution in a single-dose pen
- Injection: 0.75 mg/mL solution in a single-dose prefilled syringe
- Injection: 1.5 mg/mL solution in a single-dose prefilled syringe

4 CONTRAINDICATIONS

4.1 Medullary Thyroid Carcinoma

TRULICITY® is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see Warnings and Precautions (5.1)].

4.2 Hypersensitivity

TRULICITY® is contraindicated in patients with a prior serious hypersensitivity reaction to dulaglutide or to any of the product components. [see Warnings and Precautions (5.5)].

TRULICITY® (dulaglutide) injection, for subcutaneous use

TRULICITY® (dulaglutide) injection, for subcutaneous use

5 WARNINGS AND PRECAUTIONS

5.1 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. [see Warnings and Precautions (5.1), and Nonclinical Toxicology (13)].

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®. 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 value 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.

5.2 Pancreatitis

In Phase 2 and Phase 3 clinical studies, 12 (3.4 cases per 1000 patient years) pancreatitis related adverse reactions were reported in patients exposed to TRULICITY® versus 3 in non-insulin comparators (0.7 cases per 1000 patient years). 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 [see Dosage and Administration (2.3), Use in Specific Populations (5.6)].

5.3 Severe Gastrointestinal Disease

Use of TRULICITY® may be associated with gastrointestinal adverse reactions, sometimes severe [see Adverse Reactions (6.1)]. If a hypoglycemia reaction occurs, the patient should discontinue TRULICITY® and promptly seek medical advice.

5.4 Hypersensitivity Reactions

Systemic hypersensitivity reactions were observed in patients receiving TRULICITY® in clinical trials [see Adverse Reactions (6.1)]. If a hypersensitivity reaction occurs, the patient should discontinue TRULICITY® and promptly seek medical advice.

5.5 Renal Impairment

In patients treated with GLP-1 receptor agonists, 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 [see Dosage and Administration (2.3), Use in Specific Populations (5.6)].

5.6 Severe Gastrointestinal Disease

TRULICITY® has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

5.7 Macrocystic Outcomes

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with TRULICITY® or any other antidiabetic drug.

6 ADVERSE REACTIONS

The following serious reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-Cell Tumors [see Warnings and Precautions (5.1)]
- Pancreatitis [see Warnings and Precautions (5.5)]
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin [see Warnings and Precautions (5.2)]
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin [see Warnings and Precautions (5.3)]
- Hypoglycemia reactions [see Warnings and Precautions (5.6)]
- Severe Gastrointestinal Disease [see Warnings and Precautions (5.6)]

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Pool of Placebo-controlled Trials

The data in Table 1 are derived from the placebo-controlled trials [see Clinical Studies (6.1)]. These data reflect exposure of 1670 patients to TRULICITY® and a mean duration of exposure to TRULICITY® of 23.8 weeks. Across the treatment arms, the mean age of patients was 56 years, 1% were 75 years or older and 53% were female. This population in these studies was 60% White, 7% Black or African American, 13% Asian, 30% were of Hispanic or Latino ethnicity. At baseline, the population had diabetes for an average of 8.0 years and had a mean HbA1c of 8.0%. At baseline, 2.5% of the population reported retinopathy. Baseline estimated renal function was normal or mildly impaired (eGFR 60–90 mL/min/1.73 m²) in 96.0% of the pooled study populations.

Table 1 shows common adverse reactions, excluding hypoglycemia, associated with the use of TRULICITY® in the pool of placebo-controlled trials. These adverse reactions were not present at baseline, occurred more commonly on TRULICITY® than on placebo, and occurred in at least 5% of patients treated with TRULICITY®.
**Heart Rate Increase and Tachycardia Related Adverse Reactions.**

TRULICITY 0.75 mg and 1.5 mg resulted in a mean increase in heart rate (HR) of 2-4 beats per minute (bpm). The long-term clinical effects of the increase in HR have not been established [see Warnings and (Precautions) (5.7)].

**Adverse reactions of sinus tachycardia were reported more frequently in patients exposed to TRULICITY.** TRULICITY 0.75 mg and 1.5 mg resulted in a mean increase in heart rate of 7-9 beats per minute, respectively. 

**Neonatal Use.**

In a prenatal-postnatal study in F, maternal rats given subcutaneous doses of 0.2, 0.49, or 1.63 mg/kg every third day from implantation through lactation, F pups from F, maternal rats given 1.83 mg/kg dulaglutide had statistically significantly lower mean body weight from birth through post-natal day 63 for males and post-natal day 64 for females. F, offspring from F, maternal rats receiving 1.63 mg/kg dulaglutide had decreased forelimb and hindlimb grip strength and males had delayed balance-preparatory separation. Females had decreased startle response. These physical findings may relate to the decreased size of the offspring relative to controls as they appeared at early postnatal assessments but were not observed at a later assessment. F, female offspring of the F, maternal rats given 1.83 mg/kg dulaglutide had a longer mean escape latency and a higher mean number of errors relative to concurrent control during the training periods of 1 to 2 trials in the novel alternation test, but their mean escape latency was within the range observed in a control group. These findings occurred in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 14-fold the MRHD based on AUC. Irregular skeletal ossifications and increases in post implantation loss also were observed at 4.89 mg/kg, a systemic exposure 44-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

In pregnant rabbits given subcutaneous doses of 0.04, 0.12, or 0.41 mg/kg dulaglutide on Gestation Days 7, 10, 13, 16, and 19 (organogenesis), fetal skeletal malformations of the vertebrae and/or ribs were observed in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 13-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

In a prenatal-postnatal study in F, maternal rats given subcutaneous doses of 0.2, 0.49, or 1.63 mg/kg every third day from implantation through lactation, F pups from F, maternal rats given 1.83 mg/kg dulaglutide had statistically significantly lower mean body weight from birth through post-natal day 63 for males and post-natal day 64 for females. F, offspring from F, maternal rats receiving 1.63 mg/kg dulaglutide had decreased forelimb and hindlimb grip strength and males had delayed balance-preparatory separation. Females had decreased startle response. These physical findings may relate to the decreased size of the offspring relative to controls as they appeared at early postnatal assessments but were not observed at a later assessment. F, female offspring of the F, maternal rats given 1.83 mg/kg dulaglutide had a longer mean escape latency and a higher mean number of errors relative to concurrent control during the training periods of 1 to 2 trials in the novel alternation test, but their mean escape latency was within the range observed in a control group. These findings occurred in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 14-fold the MRHD based on AUC. Irregular skeletal ossifications and increases in post implantation loss also were observed at 4.89 mg/kg, a systemic exposure 44-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

In pregnant rabbits given subcutaneous doses of 0.04, 0.12, or 0.41 mg/kg dulaglutide on Gestation Days 7, 10, 13, 16, and 19 (organogenesis), fetal skeletal malformations of the vertebrae and/or ribs were observed in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 13-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

In a prenatal-postnatal study in F, maternal rats given subcutaneous doses of 0.2, 0.49, or 1.63 mg/kg every third day from implantation through lactation, F pups from F, maternal rats given 1.83 mg/kg dulaglutide had statistically significantly lower mean body weight from birth through post-natal day 63 for males and post-natal day 64 for females. F, offspring from F, maternal rats receiving 1.63 mg/kg dulaglutide had decreased forelimb and hindlimb grip strength and males had delayed balance-preparatory separation. Females had decreased startle response. These physical findings may relate to the decreased size of the offspring relative to controls as they appeared at early postnatal assessments but were not observed at a later assessment. F, female offspring of the F, maternal rats given 1.83 mg/kg dulaglutide had a longer mean escape latency and a higher mean number of errors relative to concurrent control during the training periods of 1 to 2 trials in the novel alternation test, but their mean escape latency was within the range observed in a control group. These findings occurred in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 13-fold the MRHD based on AUC. The human relevance of these memory deficits in the F1 female rats is not known.

It is not known whether TRULICITY is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for clinical adverse reactions from TRULICITY in nursing infants, a decision should be made whether to discontinue nursing or to discontinue TRULICITY, taking into account the importance of the drug to the mother.

**8.3 Nursing Mothers**

TRULICITY is not excreted in human milk. Because many drugs are excreted in human milk and because of the potential for clinical adverse reactions from TRULICITY in nursing infants, a decision should be made whether to discontinue nursing or to discontinue TRULICITY, taking into account the importance of the drug to the mother.

**8.4 Pediatric Use**

TRULICITY is not recommended for use in pediatric patients younger than 18 years.

**8.5 Geriatric Use**

**8.1 Pregnancy**

Pregnancy Category C

There are no adequate and well-controlled studies of TRULICITY in pregnant women. The risk of birth defects, loss, or other adverse outcomes is increased in pregnancies complicated by hyperglycemia and may be decreased with good metabolic control. It is essential for patients with diabetes to maintain good metabolic control in pregnancy and throughout pregnancy.

TRULICITY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In rats and rabbits, dulaglutide administered during the major period of organogenesis produced fetal growth reductions and/or skeletal anomalies and ossification deficits in conjunction with decreased maternal weight and food consumption attributed to the pharmacology of dulaglutide.

In pregnant rats given subcutaneous doses of 0.49, 1.63, or 4.89 mg/kg dulaglutide on Gestation Days 6, 9, 12, and 15 (organogenesis), reduced fetal weights associated with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide were observed at ≥1.63 mg/kg, a systemic exposure 11-fold to 14-fold the MRHD based on AUC. Irregular skeletal ossifications and increases in post implantation loss also were observed at 4.89 mg/kg, a systemic exposure 44-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

In pregnant rabbits given subcutaneous doses of 0.04, 0.12, or 0.41 mg/kg dulaglutide on Gestation Days 7, 10, 13, 16, and 19 (organogenesis), fetal skeletal malformations of the vertebrae and/or ribs were observed in conjunction with decreased maternal food intake and decreased weight gain attributed to the pharmacology of dulaglutide at 0.41 mg/kg, a systemic exposure 13-fold the MRHD based on AUC. No developmental adverse effects were observed at 4-fold the MRHD based on AUC.

TRULICITY is not recommended for use in pediatric patients younger than 18 years.

**8.2 Lactation**

TRULICITY is not excreted in human milk. Because many drugs are excreted in human milk and because of the potential for clinical adverse reactions from TRULICITY in nursing infants, a decision should be made whether to discontinue nursing or to discontinue TRULICITY, taking into account the importance of the drug to the mother.

**8.6 Pregnancy Category C**

TRULICITY is not excreted in human milk. Because many drugs are excreted in human milk and because of the potential for clinical adverse reactions from TRULICITY in nursing infants, a decision should be made whether to discontinue nursing or to discontinue TRULICITY, taking into account the importance of the drug to the mother.

**8.9 Patient Information**

**8.10 Human Milk**

TRULICITY is not excreted in human milk. Because many drugs are excreted in human milk and because of the potential for clinical adverse reactions from TRULICITY in nursing infants, a decision should be made whether to discontinue nursing or to discontinue TRULICITY, taking into account the importance of the drug to the mother.
8.6 Hepatic Impairment  
There is limited clinical experience in patients with mild, moderate, or severe hepatic impairment. Therefore, TRULICITY should be used with caution in these patient populations.

In a clinical pharmacology study in subjects with varying degrees of hepatic impairment, no clinically relevant changes in dulaglutide pharmacokinetics (PK) was observed [see Clinical Pharmacology (12.3)].

8.7 Renal Impairment  
In the four Phase 2 and five Phase 3 randomized clinical studies, at baseline, 50 (1.2%) TRULICITY-treated patients had mild renal impairment (eGFR ≥30 but <60 mL/min/1.73 m²), 171 (4.3%) TRULICITY-treated patients had moderate renal impairment (eGFR ≥30 but <60 mL/min/1.73 m²), and no TRULICITY-treated patients had severe renal impairment (<30 mL/min/1.73 m²). No overall differences in safety or effectiveness were observed relative to patients with normal renal function, though conclusions are limited due to small numbers.

In a clinical pharmacology study in subjects with renal impairment including end-stage renal disease (ESRD), no clinically relevant change in dulaglutide PK was observed [see Clinical Pharmacology (12.3)].

There is limited clinical experience in patients with severe renal impairment or ESRD. TRULICITY should be used with caution, and if these patients experience adverse gastrointestinal side effects, renal function should be closely monitored [see Dosage and Administration (2.3), Warning and Precautions (5.5), Clinical Pharmacology (12.3)].

8.8 Gastroparesis  
Dulaglutide slows gastric emptying. TRULICITY has not been studied in patients with preexisting gastroparesis.

10 OVERDOSAGE  
Overdoses have been reported in clinical studies. Effects associated with these overdoses were primarily mild or moderate gastrointestinal events (e.g., nausea, vomiting) and non-severe hypoglycemia. In the event of overdose, appropriate supportive care (including frequent plasma glucose monitoring) should be initiated according to the patient’s clinical signs and symptoms.

11 DESCRIPTION  
TRULICITY contains dulaglutide, a human GLP-1 receptor agonist. The molecule is a fusion protein that consists of 2 identical, disulfide-linked chains, each containing an N-terminal GLP-1 analog sequence covalently linked to the Fc portion of a modified human immunoglobulin G4 (Fab) heavy chain by a small peptide linker and is produced using mammalian cell culture. The GLP-1 analog portion of dulaglutide is 90% homologous to native human GLP-1 (7-37). Structural modifications were introduced in the GLP-1 part of the molecule responsible for interaction with the enzyme dipeptidyl-peptidase IV (DPP-IV). Additional modifications were made in an area with a potential T-cell epitope and in the areas of the IgG4 Fab part of the molecule responsible for binding the high-affinity Fc receptors and half-antibody formation. The overall molecular weight of dulaglutide is approximately 63 kilodaltons.

TRULICITY is a clear, colorless, sterile solution. Each 0.5 mL of TRULICITY solution contains 0.75 mg or 1.5 mg of dulaglutide. Each single-dose pen or prefilled syringe contains 0.5 mL of solution and the following excipients: citric acid anhydrous (0.07 mg), mmaclit (23.2 mg), polysorbate 80 (0.10 mg), trisodium citrate dihydrate (1.37 mg), in water for injection.

12 CLINICAL PHARMACOLOGY  
12.1 Mechanism of Action  
TRULICITY contains dulaglutide, which is a human GLP-1 receptor agonist with 90% amino acid sequence homology to endogenous human GLP-1 (7-37). Dulaglutide activates the GLP-1 receptor, a membrane-bound cell-surface receptor coupled to adenylyl cyclase in pancreatic beta cells. Dulaglutide increases intracellular cyclic AMP (cAMP) in beta cells leading to glucose-dependent insulin release. Dulaglutide also decreases glucagon secretion and slows gastric emptying.

12.2 Pharmacodynamics  
TRULICITY lowers fasting glucose and reduces postprandial glucose (PPG) concentrations in patients with type 2 diabetes mellitus. The reduction in fasting and postprandial glucose can be observed after a single dose.

Fasting and Postprandial Glucose  
In a clinical pharmacology study in adults with type 2 diabetes mellitus, treatment with once weekly TRULICITY resulted in a reduction of fasting and 2-hour PPG concentrations, and postprandial serum glucose incremental AUC, when compared to placebo (-25.6 mg/dL, -59.5 mg/dL, and -197 mg h/dL, respectively); these increases intracellular cyclic AMP (cAMP) in beta cells leading to glucose-dependent insulin release. Dulaglutide also decreases glucagon secretion and slows gastric emptying.

1.5 mg to steady state were approximately 19.2 L (range 14.3 to 26.4 L) and 17.4 L (range 9.3 to 33 L), respectively.

1.5 mg to steady state, the mean peak plasma concentration (C_{\text{max}}) was 37.5 ± 10.5 mg/mL, and the time to maximum plasma concentration of dulaglutide at steady-state ranges from 24 to 72 hours, with a median of 48 hours. After multiple-dose administration of 1.5 mg, the accumulation ratio was approximately 1.56. Steady-state plasma dulaglutide concentrations were achieved between 2 and 4 weeks following once weekly administration. Site of subcutaneous administration (abdomen, upper arm, and thigh) had no statistically significant effect on the exposure to dulaglutide.

The effect of dulaglutide on cardiac repolarization was tested in a thorough QTc study. Dulaglutide did not affect the QT interval.

The mean apparent clearance at steady state of dulaglutide is approximately 0.111 L/h for the 0.75 mg dose, and 0.107 L/h for the 1.5 mg dose. The elimination half-life of dulaglutide for both doses is approximately 5 days.

Specific Populations  
No dose adjustment of dulaglutide is needed based on age, gender, race, ethnicity, body weight, or renal or hepatic impairment. The effects of intrinsic factors on the PK of dulaglutide are shown in Figure 1.

Elimination – The mean apparent clearance at steady state of dulaglutide is approximately 0.111 L/h for the 0.75 mg dose, and 0.107 L/h for the 1.5 mg dose. The elimination half-life of dulaglutide for both doses is approximately 5 days.

Male  
Female

Abbreviations: AUC = area under the time-concentration curve; C_{\text{max}} = maximum concentration; ESRD = end-stage renal disease; PK = pharmacokinetics.

Note: Reference values for weight, age, gender, and race comparisons are 95 kg, 56 years old, male, and white, respectively; reference groups for renal and hepatic impairment data are subjects with normal renal and hepatic function from the respective clinical pharmacology studies. The weight values shown in the plot (70 and 120 kg) are the 10th and 90th percentiles of weight in the Phase 3 PK population.

Figure 1: Impact of intrinsic factors on dulaglutide pharmacokinetics.

Renal – Dulaglutide systemic exposure was increased by 20, 28, 14 and 12% for mild, moderate, severe, and ESRD renal impairment sub-groups, respectively, compared to subjects with normal renal function. The corresponding values for increase in C_{\text{max}} were 13, 23, 20, and 11%, respectively (Figure 1). [see Dosage and Administration (2.3), Warning and Precautions (5.5), Use in Specific Population (8.7)].

Hepatic - Dulaglutide systemic exposure decreased by 23, 33 and 21% for mild, moderate and severe hepatic impairment groups, respectively, compared to subjects with normal hepatic function, and C_{\text{max}} was decreased by a similar magnitude (Figure 1). [see Use in Specific Population (8.6)].

Drug Interactions  
The potential effect of co-administered medications on the PK of dulaglutide and vice versa was studied in several single- and multiple-dose studies in healthy subjects, patients with type 2 diabetes mellitus, and patients with hypertension.

Potential for Dulaglutide to Influence the Pharmacokinetics of Other Drugs  
Dulaglutide slows gastric emptying and, as a result, may reduce the extent and rate of absorption of orally co-administered medications. In clinical pharmacology studies, dulaglutide did not affect the absorption of the tested orally administered medications to any clinically relevant degree.

Pharmacokinetic (PK) measures indicating the magnitude of these interactions are presented in Figure 2.

No dose adjustment is recommended for any of the evaluated co-administered medications.

Abbreviations: AUC = area under the time-concentration curve; CI = confidence interval; C_{\text{max}} = maximum concentration; PK = pharmacokinetics.

Note: Reference group is co-administered medication given alone.

Figure 2: Impact of dulaglutide on the pharmacokinetics of co-administered medications.
TRULICITY (dulaglutide) injection, for subcutaneous use

In a 26-week double-blind study (26-week primary endpoint), 807 patients inadequately treated with diet and exercise, or with diet and exercise and one anti-diabetic agent at submaximal dose, were randomized to TRULICITY 0.75 mg once weekly, TRULICITY 1.5 mg once weekly, or metformin 1500 to 2000 mg daily, following a two week washout. Seventy-five percent (75%) of the randomized population were treated with one anti-diabetic agent at the screening visit. Most patients previously treated with an anti-diabetic agent were receiving metformin (≥0.5 mg/kg), increased neutrophilic inflammation of the acinar pancreas (5 mg/kg). Treatment of monkeys for 12 months with 8.15 mg/kg/twice weekly of dulaglutide (nearly 500-fold the MRHD based on AUC) demonstrated no evidence of pancreatic inflammation or pancreatic intraportal neoplasia. In 4 of 19 monkeys on dulaglutide treatment, there was an increase in goblet cells within the pancreatic ducts, but no differences from the control group in total amylase or lipase at study termination. There were no proliferative changes in the thyroid C-cells.

14.1 Monotherapy

In a 52-week double-blind study (26-week primary endpoint), 976 patients were randomized to placebo, TRULICITY 0.75 mg, TRULICITY 1.5 mg, or sitagliptin, respectively. At 26 weeks, there was a mean weight reduction of 1.4 kg, 2.7 kg, 3.0 kg, and 1.4 kg for placebo, TRULICITY 0.75 mg, TRULICITY 1.5 mg, and sitagliptin, respectively. There was a mean reduction of fasting glucose of 9 mg/dL, 35 mg/dL, 41 mg/dL, and 18 mg/dL for placebo, TRULICITY 0.75 mg, TRULICITY 1.5 mg, and sitagliptin, respectively. Treatment with TRULICITY 0.75 mg and 1.5 mg once weekly resulted in a statistically significant reduction in HbA1c compared to placebo (at 26 weeks) and compared to sitagliptin (at 26 and 52) in all combination with metformin (Table 4 and Figure 4).

Table 4: Results at Week 52 of TRULICITY Compared to Sitagliptin used as Add-On to Metformin

<table>
<thead>
<tr>
<th>ITT Population (N)</th>
<th>TRULICITY 0.75 mg</th>
<th>TRULICITY 1.5 mg</th>
<th>Sitagliptin 100 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean) a</td>
<td>8.2</td>
<td>8.1</td>
<td>8.0</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-0.9</td>
<td>-1.1</td>
<td>-0.4</td>
</tr>
<tr>
<td>Difference from sitagliptin (95% CI)</td>
<td>-0.5 (-0.7, -0.3)b</td>
<td>-0.7 (-0.9, -0.5)b</td>
<td>-</td>
</tr>
<tr>
<td>Percentage of patients HbA1c &lt;7.0%</td>
<td>49%</td>
<td>59%</td>
<td>33</td>
</tr>
</tbody>
</table>

Table 3: Results at Week 26 in a Trial of TRULICITY as Monotherapy

<table>
<thead>
<tr>
<th>ITT Population (N)</th>
<th>TRULICITY 0.75 mg</th>
<th>TRULICITY 1.5 mg</th>
<th>Metformin 1500-2000 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean) a</td>
<td>7.6</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-0.7</td>
<td>-0.8</td>
<td>-0.6</td>
</tr>
</tbody>
</table>

Fasting Serum Glucose (mg/dL) (Mean)

| Baseline | 161 | 164 | 161 |
| Change from baseline (adjusted mean) | -26 | -29 | -24 |
| Body Weight (kg) (Mean) |
| Baseline | 91.8 | 92.7 | 92.4 |
| Change from baseline (adjusted mean) | -1.4 | -2.3 | -2.2 |

Abbreviations: HbA1c = hemoglobin A1c.

a Intent-to-treat population had at least one post-baseline assessment. The primary analysis included 265 individuals in each of the treatment arms.

b Subjects included in the analysis are a subset of the ITT population that had at least one post-baseline assessment. The primary analysis included 265 individuals in each of the treatment arms.
0.75 mg, and TRULICITY 1.5 mg were blinded. After 26 weeks, patients in the placebo treatment group were randomized to either TRULICITY 0.75 mg once weekly or TRULICITY 1.5 mg once weekly to maintain study blind. Randomization occurred after a 12-week lead-in period; during the initial 4 weeks of the lead-in period, patients were titrated to maximally tolerated doses of metformin and pioglitazone; this was followed by an 8-week glycomic stabilization period prior to randomization. Patients randomized to exenatide started at a dose of 5 mcg BID for 4 weeks and then were escalated to 10 mcg BID. Patients had a mean age of 56 years; mean duration of type 2 diabetes of 9 years; 58% were male; race: White, Black and Asian were 74%, 6% and 3%, respectively; and 81% of the study population were in the US.

Treatment with TRULICITY 0.75 mg and 1.5 mg once weekly resulted in a statistically significant reduction in HbA1c compared to placebo (at 26 weeks) and compared to exenatide at 26 weeks (Table 5 and Figure 4). Over the 52-week study period, the percentage of patients who required glycemic rescue was 8.9% in the TRULICITY 0.75 mg once weekly + metformin and pioglitazone treatment group, 3.2% in the TRULICITY 1.5 mg once weekly + metformin and pioglitazone treatment group, and 8.7% in the exenatide BID + metformin and pioglitazone treatment group.

Table 5: Results at Week 26 of TRULICITY Compared to Placebo and Exenatide, All as Add-On to Metformin and Thiazolidinediones

<table>
<thead>
<tr>
<th>Intent-to-Treat (ITT) Population (N)</th>
<th>Placebo</th>
<th>TRULICITY 0.75 mg</th>
<th>TRULICITY 1.5 mg</th>
<th>Exenatide 10 mcg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean)b</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-0.5</td>
<td>-1.3</td>
<td>-1.5</td>
<td>-1.0</td>
</tr>
<tr>
<td>Difference from placebo (95% CI)</td>
<td>-0.8 (-1.0, -0.7)</td>
<td>-1.1 (-1.2, -0.9)</td>
<td>-0.5 (-0.7, -0.4)</td>
<td>-</td>
</tr>
<tr>
<td>Percentage of patients HbA1c &gt;7.0%</td>
<td>43</td>
<td>66**</td>
<td>78**</td>
<td>52</td>
</tr>
</tbody>
</table>

Add-on to Metformin and Sulfonylurea

In this 78-week (52-week primary endpoint) open-label comparator study (double-blind with respect to TRULICITY dose assignment), 807 patients were randomized to TRULICITY 0.75 mg once weekly, TRULICITY 1.5 mg once weekly, or insulin glargine once daily; all as add-on to maximally tolerated doses of metformin and glargine. Randomization occurred after a 10-week lead-in period; during the initial 2 weeks of the lead-in period, patients were titrated to maximally tolerated doses of metformin and glargine. This was followed by a 6- to 8-week glycomic stabilization period prior to randomization.

At Week 52, patients randomized to insulin glargine were started on a dose of 10 U daily. Insulin glargine dose adjustments occurred twice weekly for the first 4 weeks of treatment based on self-measured fasting plasma glucose (FPG), followed by once weekly titration through Week 8 of study treatment, utilizing an algorithm that targeted a fasting plasma glucose of <100 mg/dL. Only 24% of patients were titrated to glargine at the 52 week primary endpoint. The dose of glargine could be reduced or discontinued after randomization (at the discretion of the investigator) in the event of persistent hypoglycemia. The dose of glargine was reduced or discontinued in 28%, 52%, and 29% of patients randomized to TRULICITY 0.75 mg, TRULICITY 1.5 mg, and glargine, respectively.

Patients had a mean age of 57 years; mean duration of type 2 diabetes of 9 years; 51% were male; race: White, Black and Asian were 71%, 1% and 17%, respectively; and 0% of the study population were in the US.

Treatment with TRULICITY once weekly resulted in a reduction in HbA1c from baseline at 52 weeks when used in combination with metformin and sulfonylurea (Table 6). The difference in observed effect size between TRULICITY 0.75 mg and 1.5 mg, respectively, and glargine in this trial exceeded the pre-specified non-inferiority margin of 0.4%.

Table 6: Results at Week 52 of TRULICITY Compared to Insulin Glargine, Both as Add-on to Metformin and Sulfonylurea

<table>
<thead>
<tr>
<th>Intent-to-Treat (ITT) Population (N)</th>
<th>TRULICITY 0.75 mg</th>
<th>TRULICITY 1.5 mg</th>
<th>Insulin Glargine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean)b</td>
<td>8.1</td>
<td>8.2</td>
<td>8.1</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-0.8</td>
<td>-1.1</td>
<td>-0.6</td>
</tr>
<tr>
<td>Fasting Serum Glucose (mg/dL) (Mean)b</td>
<td>98.4</td>
<td>95.2</td>
<td>87.6</td>
</tr>
<tr>
<td>Baseline</td>
<td>161</td>
<td>165</td>
<td>163</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.3</td>
<td>-2.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Difference from insulin glargine. Adjusted mean (95% CI)</td>
<td>16 (9, 23)</td>
<td>5 (-2, 12)</td>
<td></td>
</tr>
<tr>
<td>Body Weight (kg) (Mean)a</td>
<td>86.4</td>
<td>95.2</td>
<td>87.6</td>
</tr>
<tr>
<td>Baseline</td>
<td>-2.8 (-3.4, -2.2)</td>
<td>-3.3 (-3.9, -2.7)</td>
<td></td>
</tr>
</tbody>
</table>

Add-on to Pandal Insulin, with or without Metformin

In this 52-week (26-week primary endpoint) open-label comparator study (double-blind with respect to TRULICITY dose assignment), 884 patients on 1 or 2 insulin injections per day were enrolled. Randomization occurred after a 9-week lead-in period; during the initial 2 weeks of the lead-in period, patients continued their pre-study insulin regimen but could be initiated and/or up-titrated on metformin, based on investigator discretion; this was followed by a 7-week glycomic stabilization period prior to randomization. At randomization, patients discontinued their pre-study insulin regimen and were randomized to TRULICITY 0.75 mg once weekly, TRULICITY 1.5 mg once weekly, or insulin glargine once daily, all in combination with prandial insulin lispro 3 times daily, with or without metformin. Insulin lispro was titrated in each arm based on preprandial and bedtime glucose, and insulin glargine was titrated to a fasting plasma glucose goal of <100 mg/dL. Only 26% of patients randomized to glargine were titrated to the fasting glucose goal at the 26 week primary timepoint.

Patients had a mean age of 59 years; mean duration of type 2 diabetes of 13 years; 54% were male; race: White, Black and Asian were 70%, 9% and 4%, respectively; and 33% of the study population were in the US.

Treatment with TRULICITY 0.75 mg and 1.5 mg once weekly resulted in a reduction in HbA1c from baseline. The difference in observed effect size between TRULICITY 0.75 mg and 1.5 mg, respectively, and glargine in this trial exceeded the pre-specified non-inferiority margin of 0.4%.

Table 7: Results at Week 26 of TRULICITY Compared to Insulin Glargine, Both in Combination with Insulin Lispro

<table>
<thead>
<tr>
<th>Intent-to-Treat (ITT) Population (N)</th>
<th>TRULICITY 0.75 mg</th>
<th>TRULICITY 1.5 mg</th>
<th>Insulin Glargine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean)b</td>
<td>8.4</td>
<td>8.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.6</td>
<td>-1.6</td>
<td>-1.4</td>
</tr>
</tbody>
</table>

TRULICITY (dulaglutide) injection, for subcutaneous use

TRULICITY (dulaglutide) injection, for subcutaneous use

TRULICITY TRU-0003-USPI-20150309
TRULICITY TRU-0003-USPI-20150309_TRU-0002-MG-20150309, 8 x 10.5
Table 7: Results at Week 26 of TRULICITY Compared to Insulin Glargine, Both in Combination with Insulin Lisproa (Cont.)

<table>
<thead>
<tr>
<th>Fasting Serum Glucose (mg/dL) (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRULICITY 0.75 mg</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
</tr>
<tr>
<td>Difference from insulin glargine. Adjusted mean (95% CI)</td>
</tr>
</tbody>
</table>

**Body Weight (kg) (Mean)**

<table>
<thead>
<tr>
<th>Baseline (mean)</th>
<th>Change from baseline (adjusted mean)</th>
<th>Difference from insulin glargine (adjusted mean (95% CI))</th>
</tr>
</thead>
<tbody>
<tr>
<td>91.7</td>
<td>0.2</td>
<td>-2.2 (-2.8, -1.5)</td>
</tr>
</tbody>
</table>

1. **Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data.**
2. **Least-squares (LS) mean adjusted for baseline value and other stratification factors.**
3. **Subjects included in the analysis are a subset of the ITT population that had at least one post-baseline assessment. The primary analysis included 275, 273 and 276 individuals randomized to TRULICITY 0.75 mg, TRULICITY 1.5 mg and glargine, respectively.**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

### 16.1 How Supplied

Each TRULICITY single-dose pen or prefilled syringe is packaged in a cardboard outer carton.

- **Carton of 4 Single-Dose Pens**
  - 0.75 mg/0.5 mL solution in a single-dose pen (NDC 0002-1433-80)
  - 1.5 mg/0.5 mL solution in a single-dose pen (NDC 0002-1434-80)

- **Carton of 4 Prefilled Syringes**
  - 0.75 mg/0.5 mL solution in a single-dose prefilled syringe (NDC 0002-1431-80)
  - 1.5 mg/0.5 mL solution in a single-dose prefilled syringe (NDC 0002-1432-80)

### 16.2 Storage and Handling

- **Store TRULICITY in the refrigerator at 36°F to 46°F (2°C to 8°C). Do not use TRULICITY beyond the expiration date.**
- **If needed, each single-dose pen or prefilled syringe can be kept at room temperature, not to exceed 86°F (30°C) for a total of 14 days.**
- **Do not freeze TRULICITY. Do not use TRULICITY if it has been frozen.**
- **TRULICITY must be protected from light. Storage of TRULICITY in the original carton is recommended until time of administration.**
- **Discard the TRULICITY single-dose pen or prefilled syringe after use in a puncture-resistant container.**

**17 PATIENT COUNSELING INFORMATION**

See FDA-approved Medication Guide

- **Inform patients that TRULICITY causes benign and malignant thyroid C-cell tumors in rats and that the human relevance of this finding has not been determined. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, persistent hoarseness, dysphagia, or dyspnea) to their physician [see Boxed Warning and Warnings and Precautions (5.1)].**
- **Inform patients that persistent severe abdominal pain, that may radiate to the back and which may (or may not) be accompanied by vomiting, is the hallmark symptom of acute pancreatitis. Instruct patients to discontinue TRULICITY promptly, and to contact their physician, if persistent severe abdominal pain occurs [see Warnings and Precautions (5.2)].**
- **The risk of hypoglycemia may be increased when TRULICITY is used in combination with a medicine that can cause hypoglycemia, such as a sulfonylurea or insulin. Review and reinforce instructions for hypoglycemia management when initiating TRULICITY therapy, particularly when concomitantly administered with a sulfonylurea or insulin [see Warnings and Precautions (5.3)].**
- **Patients treated with TRULICITY should be advised of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion, inform patients treated with TRULICITY of the potential risk for worsening renal function and explain the associated signs and symptoms of renal impairment, as well as the possibility of dialysis as a medical intervention if renal failure occurs.**
- **Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of GLP-1 receptor agonists. If symptoms of hypersensitivity reactions occur, patients must stop taking TRULICITY and seek medical advice promptly.**
- **Advise patients to inform their healthcare provider if they are pregnant or intend to become pregnant.**
- **Prior to initiation of TRULICITY, train patients on proper injection technique to ensure a full dose is delivered. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations.**
- **Inform patients of the potential risks and benefits of TRULICITY and of alternative modes of therapy. Inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and HbA1C testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications. During periods of stress such as fever, trauma, infection, or surgery, medication requirements may change and advise patients to seek medical advice promptly.**
- **Each weekly dose of TRULICITY can be administered at any time of day, with or without food. The day of once weekly administration can be changed if necessary, as long as the last dose was administered 3 or more days before. If a dose is missed and there are at least 3 days (72 hours) until the next scheduled dose, it should be administered as soon as possible. Thereafter, patients can resume their usual once weekly dosing schedule. If a dose is missed and the next regularly scheduled dose is due in 1 or 2 days, the patient should not administer the missed dose and instead resume TRULICITY with the next regularly scheduled dose [see Dosage and Administration (2)].**
- **Advise patients treated with TRULICITY of the potential risk of gastrointestinal side effects [see Adverse Reactions (6.1)].**
- **Instruct patients to read the Medication Guide and the Instructions for Use before starting TRULICITY therapy and review them each time the prescription is refilled. Instruct patients to inform their doctor or pharmacist if they develop any unusual symptom, or if any known symptom persists or worsens.**
- **Inform patients that response to all diabetic therapies should be monitored by periodic measurements of blood glucose and HbA1C levels, with a goal of decreasing these levels towards the normal range. HbA1C is especially useful for evaluating long-term glycemic control.**
Medication Guide

TRULICITY™ (Tru-li-si-tee) (dulaglutide)

injection, for subcutaneous use

Read this Medication Guide before you start using TRULICITY and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about TRULICITY?

TRULICITY may cause serious side effects, including:

- Possible thyroid tumors, including cancer. Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rats or mice, TRULICITY and medicines that work like TRULICITY caused thyroid tumors, including thyroid cancer. It is not known if TRULICITY will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.

- Do not use TRULICITY if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an endocrine system condition called Multiple Endocrine Neoplasia type 2 (MEN 2).

What is TRULICITY?

TRULICITY is an injectable prescription medicine that may improve blood sugar (glucose) in adults with type 2 diabetes mellitus, and should be used along with diet and exercise.

- TRULICITY is not recommended as the first choice of medicine for treating diabetes.

- It is not known if TRULICITY can be used in people who have had pancreatitis.

- TRULICITY is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.

- TRULICITY is not recommended for use in people with severe stomach or intestinal problems.

- It is not known if TRULICITY can be used with long-acting insulin.

- It is not known if TRULICITY is safe and effective for use in children under 18 years of age.

Who should not use TRULICITY?

Do not use TRULICITY if:

- you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system condition called Multiple Endocrine Neoplasia type 2 (MEN 2).

What should I tell my healthcare provider before using TRULICITY?

Before using TRULICITY, tell your healthcare provider if you:

- have or have had problems with your pancreas, kidneys or liver.

- have severe problems with your stomach, such as slowed emptying of your stomach (gastrroparesis) or problems with digesting food.

- have any other medical conditions.

- are pregnant or plan to become pregnant. It is not known if TRULICITY will harm your unborn baby. Tell your healthcare provider if you become pregnant while using TRULICITY.

- are breastfeeding or plan to breastfeed. It is not known if TRULICITY passes into your breast milk. You should not use TRULICITY while breastfeeding without first talking to your healthcare provider.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TRULICITY may affect the way some medicines work and some medicines may affect the way TRULICITY works.

Before using TRULICITY, talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking other medicines to treat diabetes including insulin or sulfonylureas.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use TRULICITY?

- Read the Instructions for Use that comes with TRULICITY.

- Use TRULICITY exactly as your healthcare provider tells you to.

- Your healthcare provider should show you how to use TRULICITY before you use it for the first time.

- TRULICITY is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. Do not inject TRULICITY into a muscle (intramuscularly) or vein (intravenously).

- Use TRULICITY 1 time each week on the same day each week at any time of the day.

- You may change the day of the week as long as your last dose was given 3 or more days before.

- If you miss a dose of TRULICITY, take the missed dose as soon as possible if there are at least 3 days (72 hours) until your next scheduled dose. If there are less than 3 days remaining, skip the missed dose and take your next dose on the regularly scheduled day.

- Do not take 2 doses of TRULICITY within 3 days of each other.

- TRULICITY may be taken with or without food.

- Do not mix insulin and TRULICITY together in the same injection.

- You may give an injection of TRULICITY and insulin in the same body area (such as, your stomach area), but not right next to each other.

- Change (rotate) your injection site with each weekly injection. Do not use the same site for each injection.

- Do not share your TRULICITY pen, syringe, or needles with another person. You may give another person an infection or get an infection from them.

Your dose of TRULICITY and other diabetes medicines may need to change because of:

- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What are the possible side effects of TRULICITY?

TRULICITY may cause serious side effects, including:

- See “What is the most important information I should know about TRULICITY?”

- inflammation of your pancreas (pancreatitis). Stop using TRULICITY and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.

- low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use TRULICITY with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin.

Signs and symptoms of low blood sugar may include:

- dizziness or light-headedness

- sweating

- confusion or drowsiness

- headache

- blurred vision

- slurred speech

- shakiness

- fast heartbeat

- anxiety, irritability, or mood changes

- hunger

- weakness

- feeling jittery

- serious allergic reactions. Stop using TRULICITY and get medical help right away, if you have any symptoms of a serious allergic reaction including itching, rash, or difficulty breathing.

- kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.

- severe stomach problems. Other medicines like TRULICITY may cause severe stomach problems. It is not known if TRULICITY causes or worsens stomach problems.

The most common side effects of TRULICITY may include nausea, diarrhea, vomiting, decreased appetite, indigestion. Talk to your healthcare provider about any side effect that bothers you or does not go away. These are not all the possible side effects of TRULICITY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of TRULICITY.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TRULICITY for a condition for which it was not prescribed. Do not give TRULICITY to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about TRULICITY. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about TRULICITY that is written for health professionals. For more information go to www.TRULICITY.com or call 1-800-545-5979.

What are the ingredients in TRULICITY?

Active ingredients: dulaglutide

Inactive ingredients: citric acid anhydrous, mannitol, polysorbate 80 and trisodium citrate dihydrate

This Medication Guide has been approved by the U.S. Food and Drug Administration.

TRULICITY is a registered trademark of Eli Lilly and Company.