Study Participant Information and Consent Form and Authorization to Use and Disclose Protected Health Information

Sponsor / Study Title:	**Eli Lilly and Company / "A Randomized, Phase 3, Open-label Trial Comparing the Effect of the Addition of Tirzepatide Once Weekly versus Insulin Lispro (U100) Three Times Daily in Participants with Type 2 Diabetes Inadequately Controlled on Insulin Glargine (U100) with or without Metformin (SURPASS-6)"**
Protocol Number:	**I8F-MC-GPHD**
Principal Investigator: (Study Doctor)	**Anuj Bhargava, M.D.**
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Introduction

You are being asked to voluntarily be in a medical research study of a study drug known as tirzepatide. Eli Lilly and Company and its representatives ("sponsor"), are sponsoring this study and are paying the study doctor and/or the study site for their work in this study.

The purpose of this form is to help you decide if you want to be in this study.

Please read this form carefully. It may contain words that you do not understand. Please ask the study doctor or nurse to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this form to think about or discuss with family or friends before making your decision. If you sign and date this form, you are giving your permission (or consent) to be a part of this study. You can agree to take part in this study and change your mind later.

If any important new information is found during this study that may affect your wanting to continue to be part of this study, you will be told about it right away.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Confidentiality of Study Information

The information in this informed consent document is intended to help you determine whether participating in this study is right for you. You may wish to discuss this information with others for the purposes of helping you decide whether to participate in the study or as needed for medical treatment. You are asked to treat this information as confidential and to inform any others with whom you share this information that it is confidential.

During the course of this study, you and/or a family member or caregiver of yours may learn, or have access to, proprietary information of the Sponsor, including drug product information. Proprietary information should be maintained as confidential. Please ask your study doctor for more specifics if you have a question about the nature of any particular information.

Why is this study being done?

The main reason for you to take part in this study is not to treat you for your condition but to help in answering the following research questions:

- The safety of tirzepatide and any side effects you might have when you take it.
- Whether tirzepatide can help study participants with type 2 diabetes.
- Whether tirzepatide is tolerable when taken with insulin glargine.
- How much tirzepatide should be given to study participants.
- How tirzepatide compares to insulin lispro.

This study is being done to see how safe an investigational drug is and how well it will work to help people with type 2 diabetes. "Investigational" means that the drug being tested has not been approved for routine clinical use or for the use described in this study by the United States Food and Drug Administration (FDA). The FDA is allowing the use of this drug for research.

How many people will take part in the study?

Approximately 1182 study participants will be taking part in this study.

What will happen during the study?

You will be asked to:

- Sign and date this consent form;
- Give your health history. The study staff will review your medical history and test results to see if you can be part of this study.
- Tell the study staff if you take any over-the-counter or prescription drugs, vitamins, or herbs.

The study staff will discuss what is required for you to be part of this study.

You cannot take part in this study if:

- You have Type 1 diabetes.
- You have a history of pancreatitis (inflammation of the pancreas).

- You have a history of retinopathy (damage to the blood vessels of your eyes), which your study doctor will discuss with you.
- You have a history of diabetic macular edema (swelling in the retina of your eye), which your study doctor will discuss with you.
- You have a history of severe hypoglycemia (very low blood sugar), which your study doctor will discuss with you.
- You are taking certain medications, which your study doctor will discuss with you.
- You have had, or plan to have, a weight loss procedure such as gastric bypass or a Lap-Band®.
- You have conditions that affect the emptying of your stomach, which your study doctor will discuss with you.
- You have a history of diabetic ketoacidosis (a buildup of acid in the bloodstream due to uncontrolled blood sugar), which your study doctor will discuss with you.
- You have had a heart attack, stroke, or heart failure, which your study doctor will discuss with you.
- You have hepatitis.
- You or someone in your family has a history of thyroid cancer, which your study doctor will discuss with you.
- You have a history of an active or untreated cancer, which your study doctor will discuss with you.
- You are pregnant or breast feeding.
- You have been treated with drugs that promote weight loss, which your study doctor will discuss with you.
- You are enrolled in any other clinical trial.

You may need to have some exams or tests done to find out if you are a candidate to begin the study drug. Some of these tests may be done even if you do not join the study as part of your normal care.

At Visit 2, you are required to:

- Stop taking oral glucose lowering medications other than metformin (if you were using it), and
- Switch your basal insulin (long acting insulin) therapy to insulin glargine (a long acting insulin) daily at bedtime, which will be provided to you.

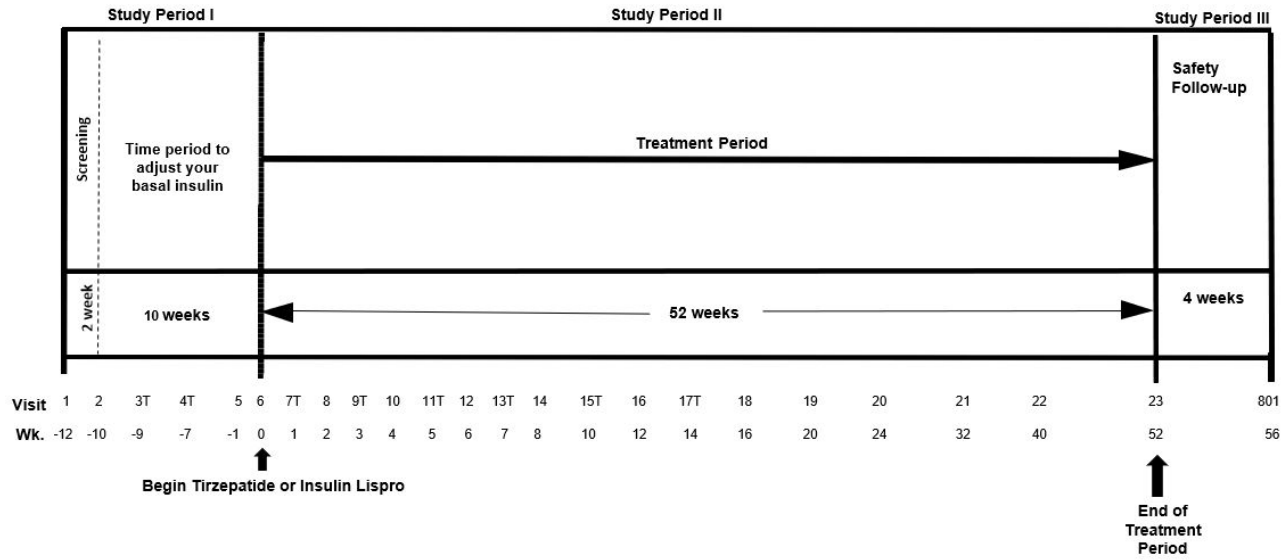
Your study doctor will provide you with proper instructions on adjusting the dose of insulin glargine between Visit 2 and Visit 6 (randomization visit) per your requirement.

You will be required to continue insulin glargine and metformin (if you were using it) for the entire study.

Dose of insulin glargine is required to be adjusted throughout the study depending on your morning blood glucose levels. Your study doctor will provide you proper instructions on adjusting the dose of insulin glargine.

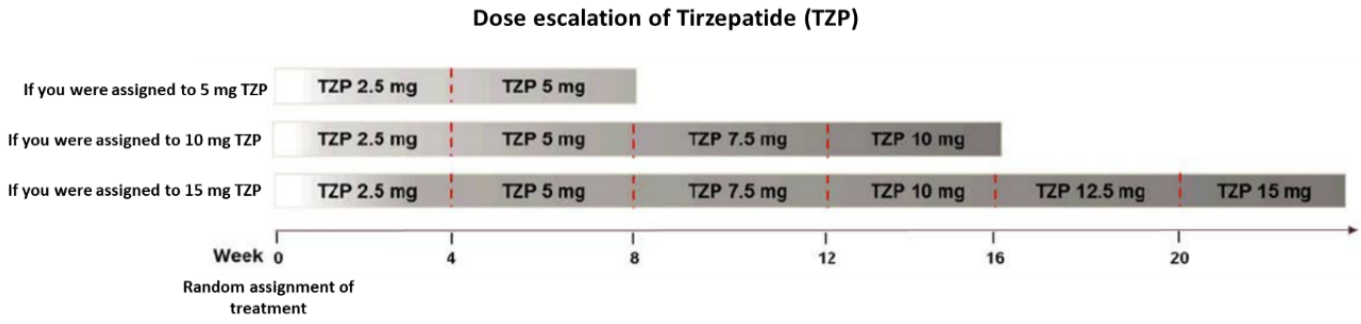
At Visit 6, you will get tirzepatide or insulin lispro (a short acting insulin). You will know which study drug you are taking. Whether you receive tirzepatide or insulin lispro will be decided by chance. The chance that you will receive tirzepatide is 1 in 2.

If you get Tirzepatide, it is required to be injected once weekly. You will be assigned to either 5 mg, 10 mg, or 15 mg tirzepatide group.



Abbreviation: T = telephone

You will gradually increase the dose of tirzepatide to reach the dose you are assigned. See the diagram below explaining the dose escalation of tirzepatide.



If you get insulin lispro, it is required to be injected three times a day before three largest meals of the day (for example, breakfast, lunch and dinner).

Dose of insulin lispro is required to be adjusted throughout the study depending on your pre-meal glucose levels and bed-time glucose levels. Your study doctor will provide you proper instructions on adjusting the dose of insulin lispro.
You will be monitoring your blood glucose very closely throughout this study. Your study doctor will provide you proper instructions.

You will:

- Use the study drug only as instructed by the study staff;
- Return any unused study drug and containers at the end of this study, or as instructed by the study staff;
- Give yourself the study drug by subcutaneous injection (under the skin)

It is important that you are completely truthful with the study staff about your health history. You should not take part in this study if you do not meet all requirements.

Total participation will be about 68 weeks. Screening and insulin adjustment will be about 12 weeks, study treatment will be about 52 weeks, and safety follow-up will be about 4 weeks.

Please review the table below. This will give you information about what will happen at each specific visit and how often the procedures will happen.

Schedule of Activities

Screening:

Activity	Screening/Insulin Optimization					Comments
Visit Number	**1**	**2**	**3**	**4**	**5**	Your study doctor will determine whether you need Visit 4 a visits are not required, you will skip all activities performed
Weeks before starting study treatment	**-12**	**-10**	**-9**	**-7**	**-1**	
Visit interval tolerance (days)	**--**	**±3**	**±3**	**±3**	**±3**	
Telephone Visit			**X**	**X**		
Sign and date informed consent	X					Must sign and date before beginning procedures.
Talk to your study doctor about your health	X					This will include your medical history.
Talk to your study doctor about your current medication and any harmful affects you may experience	X	X	X	X	X	
Have a physical examination	X				X	This may include weight, height, heart rate, and blood press
Have an eye exam		X				
Talk to your study doctor about your diabetes and the supplies you will be using		X				Includes counseling on diet and exercise, symptoms and mar hypoglycemia, etc.
Receive your supplies		X			X	
Receive training on your insulin pen		X				
Take home your diary		X				
Talk to your study doctor about the 7-point self-monitoring blood glucose test			X		X	See note below.
Have your blood drawn (about-mL)	15				6	Includes pregnancy testing for women of child bearing poten
Receive your insulin glargine		X			X	
Talk to your study doctor about your insulin glargine dosing			X	X	X	

Note: Your study doctor will tell you at Visit 3 or Visit 5, when to collect 7-point self monitored blood glucose test

You will need to check your blood sugar using blood sugar monitor that will be provided to you at Visit 2. You will need to do so seven times in 1 day on 2 separate days in one week. This is done by:

- Checking your blood sugar before and 2 hours after your first meal (for example, breakfast),
- Checking your blood sugar before and 2 hours after your second meal (for example, lunch),
- Checking your blood sugar before and 2 hours after your third meal (for example, dinner), and
- Once more before bedtime.

Study Treatment:

Activity	Study Treatment Period																		
Visit Number	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**ET**
Weeks from starting study treatment	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**10**	**12**	**14**	**16**	**20**	**24**	**32**	**40**	**52**	
Study day	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**57**	**71**	**85**	**99**	**113**	**141**	**169**	**225**	**281**	**365**	
Visit interval tolerance (days)	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±3**	**±7**	**±7**	**±7**	
Fasting Visit	**X**		**X**		**X**				**X**		**X**		**X**	**X**	**X**		**X**	**X**	**X**
Telephone Visit		**X**		**X**		**X**		**X**		**X**		**X**							
Talk to your study doctor about your current medication and any harmful affects you may experience	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Have a physical exam	X		X		X		X		X		X		X	X	X	X	X	X	X
Have an electrocardiogram	X																X	X	X
Talk to your study doctor about your diabetes and the supplies you will be using	X																		
Receive your supplies	X		X		X		X		X		X		X	X	X	X	X	X	X
Receive training on your insulin pen or tirzepatide single-dose pen	X																		
Receive your diary	X				X				X		X		X	X	X	X	X	X	X
Talk to your study doctor about the 7-point self monitoring blood glucose test														X		X	X		
Return your diary	X		X		X		X		X		X		X	X	X	X	X	X	X
Answer questionnaires	X																	X	X
Have your blood drawn (about-mL)	40		3		6				6		38		6	6	38		40	40	40

Urine pregnancy test	X										X				X		X	X	
Provide a urine sample	X										X				X		X	X	X
Receive your study drug	X		X		X		X		X		X		X	X	X	X	X	X	X
Talk to your study doctor about your insulin dosing	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Return your study drug and supplies	X		X		X		X		X		X		X	X	X	X	X	X	X

[1]**Early Termination**- If you are unable or unwilling to continue in the study for any reason, you will perform an Early Termination visit

Note: Your study doctor will tell you at the marked visits, when to collect 7-point self-monitored blood glucose test
You will need to check your blood sugar using blood sugar monitor that will be provided to you at Visit 2. You will need to do so seven times in 1 day on 2 separate days in one week. This is done by:

- Checking your blood sugar before and 2 hours after your first meal (for example, breakfast),
- Checking your blood sugar before and 2 hours after your second meal (for example, lunch),
- Checking your blood sugar before and 2 hours after your third meal (for example, dinner), and
- Once more before bedtime.

Follow-Up Period:

Activity	**Follow-Up Period**	**Comm**
Visit Number	**801**	
Weeks from study treatment	**4 weeks after end of study treatment**	
Visit interval tolerance (days)	**±7**	
Fasting Visit	**X**	
Talk to your study doctor about your current medication	X	
Talk to your study doctor about any harmful affects you may experience	X	
Have a physical exam	X	This may include weight, waist circu pressure.
Have an electrocardiogram	X	
Return your diary	X	
Have your blood drawn (about-mL)	40	
Urine pregnancy test	X	Only for women of childbearing po
Provide urine	X	

Are samples being collected?

Please review the information below. This explains what samples are being collected, how they will be used, and how long they will be stored. Additional samples may be required to repeat a test if needed. The samples and any data generated from the sample can only be linked back to the study participant by the study site staff.

General Information Regarding Sample Collection

Various blood and urine samples will be collected from you during this study. The specific procedures for collecting these samples and the risks associated with collection are explained in the procedure table and risks section in this document. Your samples will be identified by your study participant number, and not by your name.

The analysis of your sample(s) may contribute to the creation of new laboratory tests, new medicines, or other items that may be commercially valuable to the sponsor. The sponsor has no plans to provide you, either now or in the future, any compensation, royalty, or any other financial benefit that might result from any product, procedure, or other item that may be developed from studying your sample(s) or any information or data that is derived from such research.

Samples for Study Qualification and Health Monitoring

Blood and urine samples will be collected to determine if you meet the requirements to participate in this study.

Additional blood and urine samples will be collected throughout the study to monitor your health and your response to study drug.

Blood samples may be tested for Hepatitis A, B, C, or E which are serious and contagious diseases. If your test results are positive, your study doctor or staff will contact you.

The results of Hepatitis A, B, C and/or E testing will be kept confidential and disclosed only as required by law.

All samples collected for Study Qualification and Health Monitoring **will be destroyed within 60 days of confirmation of the test results, unless laws, regulations,** or international **laboratory certification standards require a longer retention period.** This confirmation will either occur immediately after initial testing, or may require that samples be held to be retested at a defined later point in time.

Samples for Biomarker Research

Sometimes scientists measure substances in the body to diagnose, evaluate, or monitor a person's medical condition or disease. For example, cholesterol levels in the blood can be used to monitor a person's risk for heart disease. In this example, cholesterol is a biomarker.

Blood will be collected to identify or better understand biomarkers.

Researchers may use biomarkers to learn more about type 2 diabetes or how study participants respond to study drug or other medicines that you are taking during this study. Your sample(s) may also be used to create or improve tests to help identify study participants in the future who may respond to this study drug.

These biomarker samples may also be used to measure the amount of study drug that is in your body and how your body breaks it down, or to determine if your body produces antibodies against the study drug. Antibodies may affect how a drug works in your body if you take it in the future.

The sample(s) may be stored for up to **15** years after this study is finished.

Other Samples

If you experience an injection site reaction or a reaction from your immune system (such as hives or a severe allergic reaction**),** additional blood samples will be collected to determine if your body produces antibodies against the study drug. Antibodies may affect how a drug works in your body if you take it in the future. The sample(s) may be stored for up to **15** years after this study is finished.

What will happen when I am finished with the study?

The study doctor or one of the study staff members may try to reach you after you have stopped study treatment. They will want to talk to you to see how you are doing. They may also want to ask about any other treatment you received since leaving this study. If you move or lose contact with the study doctor and staff, they may give your name and last known contact information to a third party vendor to try to find your current contact information.

What side effects or risks can I expect from being in the study?

There may be risks to you if you are in this study.

During the study, you will continue to take your metformin (if you were already on it at the start of the study). Ask your study doctor about any risks that may be associated with your metformin. Your study doctor may suggest continuing the medication at the same dose.

During the study, you may be advised to take medication to treat symptoms that may arise during the study. The study doctor will discuss any risks with you.

Risk profile for Tirzepatide:

As of 15 June 2018, 338 adults with type 2 diabetes and 67 healthy adults have taken tirzepatide in completed studies. Many of these participants were considered overweight or obese. Lilly has reviewed safety information from these studies.

Cases of pancreatitis have been reported in participants with type 2 diabetes who have taken tirzepatide and other glucagon-like peptide-1 receptor (GLP-1) medicines. Pancreatitis is an

inflammation of the pancreas, a gland in your abdomen that helps with digestion. Pancreatitis is usually associated with stomach pain, which may be severe. Although pancreatitis usually improves without long-term effects, it may be severe and could lead to hospitalization or even death.

If you develop abdominal pain that is not normal for you, or if you develop severe nausea with or without vomiting, you should call your study doctor immediately for evaluation and proper care. If you have pancreatitis symptoms or if routine laboratory tests suggest a need for evaluation, you may be asked to return to the study site for further evaluations, which may include additional blood tests, X-rays, or other abdominal pictures.

Symptoms of nausea, vomiting, and diarrhea may lead to loss of fluids (dehydration). The loss of fluids could worsen kidney function, which includes kidney failure, and requires immediate evaluation by the study doctor for appropriate care.

Tirzepatide is not recommended for participants with severe stomach problems, such as slowed emptying of the stomach (gastroparesis) or problems with digesting food.

Increases in resting heart rate above the normal range (more than 100 beats per minute) have been seen in both healthy participants and participants with type 2 diabetes taking tirzepatide. Increased HR can have no symptoms or symptoms such as pounding heart, irregular or "skipped" heartbeat that you can feel, chest pain, or other more severe symptoms. Your heart rate, blood pressure, and electrical recordings of the heart (electrocardiograms) may be checked regularly.

If you take tirzepatide with or without other medicines used to treat type 2 diabetes, your blood sugar could become too low (hypoglycemia). While taking tirzepatide, you may be more likely to have low blood sugar if you are also taking insulin or an insulin secretagogue (sulfonylurea). It is important to follow the study doctor's recommendations for monitoring your blood sugar level during your participation in this study. You should tell the study doctor if you experience any symptoms of low blood sugar, such as sweating, hunger, shakiness, or confusion.

Cases of severe and potentially life-threatening allergic reactions have occurred rarely in participants taking other GLP-1 medicines and may be a potential side effect with tirzepatide. Tirzepatide should not be given to participants who have had a serious allergic reaction to tirzepatide or any of its ingredients.

Your body's disease protection system (immune system) may react to tirzepatide by making antibodies. Your study doctor may take blood samples during the study to check for antibodies to tirzepatide.

Very rarely, cases of medullary thyroid cancer were reported with other GLP-1 medicines. If you or anybody from your family (genetic relatives only) have had this type of cancer or another disease called multiple endocrine neoplasia syndrome type 2, please tell your study

doctor because you should not receive tirzepatide. If you are participating in a long-term study with tirzepatide, your calcitonin levels may be measured.
Additionally, it is possible that you could have other unknown side effects while taking tirzepatide.

You should not take tirzepatide if you are pregnant or may become pregnant. Female rats that were given tirzepatide had irregular menstrual cycles and body weight loss or decreased body weight gain or both. Pregnant rats and rabbits that were given tirzepatide and lost too much body weight had offspring that were smaller than normal. Some of these offspring had malformations (organ development abnormalities). Because tirzepatide has only been tested in pregnant animals, humans who take tirzepatide while pregnant may experience other unknown side effects.

Very Common (affects 10 or more out of 100 people)	**Common** (affects 1 or more out of 100 people)	**Uncommon** (affects 1 or more out of 1000 people)
● Feeling sick to the stomach ● Loose or frequent stools ● Throwing up, vomiting ● Loss of appetite	● Headache ● Dizziness ● Indigestion ● Heartburn ● Feeling tired, fatigue ● Hard or infrequent stools ● Passing gas ● Bloating ● Belching ● Stomach pain or discomfort ● Weight loss ● Low blood sugar	● Feeling full quickly when eating

Risk profile for Insulin Glargine:

As of 21 April 2019, cumulative patient exposure of insulin glargine (LY2963016) totaled 1507 patients. LY2963016 is an insulin product, approved for the treatment of diabetes. LY2963016 is highly similar (biosimilar) to another product that is already available on the market, called LANTUS® (insulin glargine, Sanofi-Aventis, Bridgewater, NJ). LY2963016 is a kind of insulin with the same active ingredient found in LANTUS®. LY2963016 and LANTUS® are made using different methods. This could result in slight differences between the 2 products overall. LY2963016 is expected to work in the same way and have the same effect in people as LANTUS®. LANTUS® has been used for over 13 years in people with diabetes to lower blood sugar. The effects of LANTUS® can last for up to 24 hours. Because LANTUS® lasts for a long time, it lowers blood sugar level for a longer period of time than short-acting insulins.

A common experience reported by those taking any insulin, including LY2963016, is low blood sugar, which could cause lack of energy, hunger, confusion, pounding heart, sweating, shakiness, and headache. Low blood sugar may occur overnight. Patients may also have

blood sugar low enough that they cannot treat themselves. Severe cases of low blood sugar could cause unconsciousness, and in extreme cases, death.

In clinical studies comparing LY2963016 and LANTUS® in participants with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM), the side effects of the 2 drugs were shown to be highly similar. These side effects are described in the table below. No new side effects were seen in the clinical studies with LY2963016.

There may be redness, pain, swelling, itching, or hives where the insulin is injected. Pain where the insulin is injected happens in about 3 out of every 100 people who take LANTUS®. Sometimes, a dimple or thickening in the skin can form over time if you always inject in the same place. To help prevent these side effects, change where you inject your insulin each time.

As with other insulins, your body's immune system (disease-protection system) may react to insulin glargine by making proteins (antibodies) that react with foreign substances in your body. Antibodies formed against insulin glargine could cause an allergic reaction or could interfere with how the body normally responds to insulin (insulin resistance). Blood samples may be taken in some studies to see if antibodies to insulin glargine are being formed. Participants taking any insulin, including insulin glargine, may experience a generalized allergic reaction to insulin, a very rare, but possibly life-threatening event.

You can inject insulin using a syringe or a pen-type device. If you use a pen-type device, you must read the instructions provided before using the pen. You must also carefully follow the directions. If you do not follow the directions that come with the pen, or if you use the pen incorrectly (which may result in a broken, damaged, or jammed pen), you may receive too much or too little insulin. This may result in low blood sugar or high blood sugar. If any part of the pen looks like it is damaged or broken, do not use the pen and return it to your study coordinator. A pen that does not work properly may deliver too much or too little insulin, even if you follow the directions exactly. The choice of a syringe or pen will not change the risks described for insulin.

Sometimes, other medicines you are taking can affect how well LANTUS® or insulin glargine works to lower your blood sugar. Your study doctor will tell you what drugs can be taken while taking insulin glargine. Be sure to tell your study doctor about all medicines, even over-the-counter medicines (medicines you can buy without a prescription) you are currently taking.

Insulin treatment can cause you to gain body weight. This side effect is expected with both LANTUS® and insulin glargine.

Many people can treat their low blood sugar levels by themselves. This can be done by drinking or eating a food with carbohydrates ("carbs"). Severe low blood sugar is a situation in which a person cannot treat low blood sugar by himself or herself. That is, another person needs to help treat the severe low blood sugar level.

Severe low blood sugar level was seen in about 2 out of 100 adults with type 2 diabetes taking LANTUS® and oral agents for up to 1 year.

Severe low blood sugar was seen in about 8 out of 100 adults taking LANTUS® and regular insulin for 5 years. In participants with type 2 diabetes, about 1 out of 200 patients taking insulin glargine and oral agents had episodes of severe low blood sugar level over 24 weeks.

Risks in Pregnant, Nursing Mothers, and Older Population

Insulin glargine has not been studied in pregnant animals. The effects of insulin glargine in pregnant animals should be similar to other kinds of insulin, including LANTUS®. Birth defects have been found in baby animals when mothers were treated with other kinds of insulin during pregnancy. These birth defects are thought to be due to severe low blood sugar episodes in pregnant animals getting other kinds of insulin. More modest doses of other kinds of insulin produced less severe and temporary decreases in blood sugar. These more modest doses did not cause birth defects. There are no clinical studies of the use of LANTUS® in pregnant women. Pregnant or nursing mothers are not planned to be included in studies with insulin glargine. If you are pregnant or plan to become pregnant during the study, you should not participate in the study. Women who are able to conceive a child should use birth control methods approved by their doctor during clinical studies.

In studies in participants who were taking LANTUS® or NPH insulin, participants older than 65 years had more events involving the heart and blood vessels than the population as a whole.

Very Common (affects 10 or more out of 100 people)	**Common** (affects 1 or more out of 100 people)	**Uncommon** (affects 1 or more out of 1000 people)	**Rare** (affects 1 or more out of 10,000 people)	**Very Rare** (affects less than 1 out of 10,000 people)
• Low blood sugar	• Thickening of skin tissue • Redness, pain, swelling, or itching at injection site	• Thinning of skin tissue	• Allergic reactions • Swelling • Problems with eyesight	• Loss of taste • Muscle pain

Risk language for insulin lispro (Humalog Kwikpen):

As of 30 April 2018, cumulative patient exposure of Lilly's insulin analogs (lispro products) totaled approximately 92.1 million patient-years.

A common experience reported by those taking any insulin, including insulin lispro is low blood sugar, which could cause lack of energy, hunger, confusion, pounding heart, sweating, shakiness, and headache. Low blood sugar may occur overnight. Participants may also have a blood sugar low enough that they cannot treat themselves. Severe cases of low blood sugar could cause unconsciousness, and in extreme cases, death.

Occasionally, participants taking any insulin may experience weight gain, swelling due to fluid retention, or redness, swelling, or itching where the insulin is injected.

Rarely, a dimple or depression in the skin or an enlargement or thickening of the tissue under the skin may form over time if the insulin is always injected in the same place. Participants taking any insulin may experience a generalized allergic reaction to insulin, a very rare, but possibly life-threatening event.

The risk of low blood sugar after taking insulin lispro can be lowered if you eat food within 15 minutes of injecting your insulin and if you do not do heavy exercise for 2 hours after your injection.

Read the Instructions for Use (IFU) for the syringe or pen-type device before use.

Procedure Risks

Blood Tests
For most people, needle punctures for blood draws do not cause any bad problems. However, sometimes they may cause bleeding, bruising, discomfort, infections and/or pain where you had the blood drawn. You may also feel dizzy.

Electrocardiograms (ECGs)
There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin

Glucose Monitoring
Blood sugar testing requires pricking your finger and testing a drop of blood. This does not usually cause serious problems, but it can cause some discomfort.

Subcutaneous Injection (injections under the skin)
For most people, needle punctures for injections under the skin do not cause any serious problems. Sometimes they may cause bleeding or bruising where the shot is given. Sometimes people complain of discomfort, infections and/or pain at the site of the shot. Infection may happen with injections under the skin because the needle breaks the skin. Then germs can get into the skin underneath. Shots may cause abscesses or skin and soft tissue infections. Additionally, if a blood vessel is hit by the needle, the risk of infection will be even greater if germs are taken into the blood system.

Insulin injections may cause:

- redness,
- pain,
- swelling,
- itching
- hives
- your skin may become thicker at the site if you always inject in the same spot.

Over time, you may also develop a reaction to taking insulin. It could interfere with how your body reacts to insulin.
This could lead to low or high blood sugar, which would require insulin dose adjustments.
Rarely, you may have an allergic reaction which may be life-threatening.

Eye Exam

You may receive drops in your eyes during your eye exam that will dilate your pupils (small openings in the middle of your eyes). Dilated pupils may make it difficult for you to drive, work in bright light, or read for a while after your appointment.

Please talk to the study doctor or staff about any questions or concerns that you may have about the procedures required for this study.

What are the Reproductive Risks?

If you are female, you should not become pregnant or breastfeed a child while in this study. Naturally, the best way to not become pregnant is not to have vaginal sex (intercourse). If you are sexually active, you must use birth control. You should talk with your study doctor about the types of birth control that are best for you and your partner. Tell your study doctor right away if you become pregnant or think you are pregnant. The study staff will collect information about the pregnancy, its outcome, and the health of the child after birth.

You are not required to use contraception if you are a woman in an exclusively same-sex relationship(s).

If you are male, you should not father a baby while in this study. You should not have vaginal sex (intercourse) without using effective birth control. Talk to your study doctor about the types of birth control that might be best for you and your partner. Tell the study doctor right away if your partner becomes pregnant or thinks she may be pregnant. She will be asked to sign a separate consent form to allow the study staff to collect information about the pregnancy, its outcome, and the health of the child after birth. Also, you should not donate semen/sperm.

You are not required to use contraception if you are a man in an exclusively same-sex relationship(s).

Taking part in this study can result in risks to an unborn child or breastfeeding child. If you are a female, you must continue to use birth control throughout the study and for 30 days after the study if you are sexually active. If you are a male, you should not donate semen/sperm and follow the contraceptive requirements throughout the study and for 90 days after the last dose of the study drug.

There may also be unknown risks to your embryo, fetus, or nursing child.

Other Risks

In addition to the side effects already described tirzepatide, insulin glargine, insulin lispro, and the study procedures may have other unknown risks.

There may be unknown risks of possible harmful interaction with other medication you may be taking.

You should not give the study drug to other people and should keep it out of the reach of small children.

Are there benefits to taking part in the study?

You may or may not receive any benefit from being in this study. If you take part in this study, other people with type 2 diabetes may be helped.

Information obtained from this study will also benefit the sponsor of the study and may benefit study participants in the future. You may receive information from physical examinations, laboratory tests, or other testing that is done in this study but these tests may not have any impact on your health.

What other choices do I have if I do not take part in this study?

You do not have to take part in this study to be treated for your condition. Other treatments for your condition are available.

Your other choices may include:

- Getting treatment or care for your type 2 diabetes without being in a study
- Insulin or other glucose lowering drugs
- Special diet or other lifestyle changes

What happens if I want to stop the study?

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time. You may do so without a penalty or loss of benefits to which you are otherwise entitled.

Your participation also may be stopped by the study doctor or sponsor for any reason without your consent. If this happens, it might be due to a bad reaction you have to tirzepatide or new information about tirzepatide safety or effectiveness.

If you stop being part of this study, the study doctor or one of the staff members will talk to you about any medical issues regarding the stopping of your participation.

What are the costs of taking part in this study?

Study drug and study procedures will be provided at no cost to you.

You are invited to voluntarily take part in an optional program to reimburse you for your study inconvenience fees and travel expenses. You do not have to participate or you can also decide to stop participating at any time.

Participant inconvenience Fees:

You will be provided fixed amounts, as outlined below, for inconvenience fees related to time spent (for example, lost wages) and burden of the study:

- **For Clinic Visits, Phone Visits, and Diary Entry:**
    - $75 per visit, applicable to Visits 1, 3, 7, 9, 11, and 13
    - $125 per visit, applicable to Visits 4, 8, 10, 12, 14, 15, and 17
    - $150 per visit, applicable to Visits 2 and 6
    - $175 per visit, applicable to Visits 16 and 18
    - $275 per visit, applicable to Visits 19, 20, and early termination (ET) visit if applicable
    - $250 for Visit 801
    - $375 for Visit 5
    - $475 per visit, applicable to Visits 21 and 22
    - $675 for Visit 23
- **For Unscheduled Visits**
    - $75 per Visit

Caregiver Inconvenience Fees:

You will be provided fixed amounts, as outlined below, for caregiver inconvenience fees related to time spent (for example, lost wages) and burden of the study:

- $75 for Visit 2 (scheduled and unscheduled dilated fundoscopic exams)

You may be reimbursed actual expenses for all study visits completed on the items indicated below:

- **Transportation**: Reimbursed at least the minimum standard IRS mileage rate for medical transportation to cover transportation from your home address to the nearest study treatment center at time of enrollment. The IRS mileage rate may change periodically.

- **Public transportation** (taxis, bus, train, subway): When mileage is NOT being paid, you will receive up to $100. You will be reimbursed the actual amount up to the maximum amount per round trip visit. Car rental is not included in this coverage. Receipts are required.

- **Parking fees and tolls** (if applicable): There is a $50 maximum limit per visit. You will be reimbursed the actual amount up to the maximum amount. Parking fees will not be reimbursed if the cost is covered by the site. Receipts or other supporting documentation are required if applicable/available.

- **Meal reimbursement**: provided for fasting visits and/or visits greater than 3 hours (V6, V8, V10, V14, V16, V18, V19, V20, V22, V23, V801, and early termination, if applicable), up to $25/meal.

- **Additional Participant Meals:** provided for Visit 6 if greater than 3 hours with excessive travel (greater than 90 miles, roundtrip), up to $25/meal.

- **Hotel stay reimbursement**: for you and your caregiver. Provided at Visit 6 if visit is greater than 3 hours and involves excessive travel (greater than 90 miles, roundtrip). You will be reimbursed the actual amount up to $200 per night. Reimbursement may not cover the entire hotel rate. Receipts are required.

Note: The IRS requires that compensation (not documented by receipts or other tracking methods) greater than or equal to $600 be reported to the IRS as required by law. Refer to http://www.irs.gov/pub/irs-pdf/i1099msc.pdf.

If you do not finish the study, you will be reimbursed for the part of the study that you did complete. However, your expenses could be more than the amount you are reimbursed.

More information about reimbursement is in the Study Participant Reimbursement Information Sheet.

What happens if I am injured because I took part in this study?

If you are injured, please seek medical help. If you follow the directions of the study doctor and staff, the sponsor will pay the medical expenses for the treatment of a physical injury because of a properly given drug or procedures. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

Who should I contact if there is an emergency or if I have questions?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants.

If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00043260.

Will my medical information be kept private?

The study doctor and staff will handle your personal health information in a confidential manner.

By signing and dating the consent document for this study, you give permission ("authorization") for the uses and disclosures of your personal health information in the following ways.

- Your original medical records (which may contain your full name or other information that may directly identify you) may be shared with or viewed by to ensure the quality of the study conduct and study data:
  - The sponsor of the study and its representatives "sponsor",
  - the regulatory authorities in this country (such as the U.S. Food and Drug Administration) and in other countries, and
  - the institutional review board overseeing this study.
- Your study data (information collected for the study which only identifies you by a code and not your full name or other information that may directly identify you) may be shared with or viewed by:
  - the sponsor and their business partners (including those in other countries),

- When the sponsor shares any data outside of this country, the sponsor will respect the terms of this data privacy statement even if other countries may have privacy laws that do not provide the same protections
- The sponsor will only share your study data with their business partners, only if they need the information as a part of this work with the sponsor. The business partners must sign a contract that requires it to protect your study data in the same way as the sponsor.

  - the regulatory authorities in this country (such as the U.S. Food and Drug Administration) and in other countries,
  - the institutional review board overseeing this study, and
  - the doctors at other institutions participating in the study.

- The sponsor will use the study data:
  - to support the study purposes described in the consent document,
  - to determine how safe or effective any of the drugs or treatments included in the study,
  - to better understand the disease(s) included in the study, or
  - to improve the design of future studies.
- Study data that does not directly identify you may be published.

Your personal health information may no longer be protected under the HIPAA privacy rule once it is disclosed by your study doctor to these other parties.

You have the right to see and copy your personal health information related to the research study. However, you may not be able to review some of the study data until after the study has been completed to ensure the scientific integrity of the study.

Your authorization for the uses and disclosures of your personal health information does not have an expiration date. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign and date this authorization document.

You may cancel your authorization for the uses and disclosures of your personal health information at any time by providing written notice to the study doctor. If you cancel your authorization:

- The study doctor and staff will only use or disclose some of your personal health information if it is needed to confirm the accuracy of the study data.
- The sponsor will still use study data that was collected before you cancelled your authorization.
- You will no longer be able to participate in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Subject

_____ _____

Signature of Subject Date

_____

Printed Name of the Person Obtaining the Authorization

_____	_____
Signature of the Person Obtaining the Authorization	Date

Study Participant Information and Consent Form

Signature Page

To become a part of this study, and to authorize use and disclosure of your personal health information, you or your legal representative, if applicable must sign and date this page.

Only sign and date this consent after:

- You have read all of the information in this Study Participant Information and Consent Form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.

You voluntarily agree to be part of this research study, and to do the following:

- To follow the study procedures, and
- To provide necessary information to the study doctor, nurses, or other staff members, as requested.

You may freely choose to stop being a part of this study at any time. You will receive a copy of this signed and dated Study Participant Information and Consent Form to keep.

FOR STUDY PARTICIPANT TO COMPLETE

Signature of Study Participant	Date (Study Participant must personally date)
Study Participant Name (print or type)	

FOR INDIVIDUAL CONDUCTING INFORMED CONSENT DISCUSSION TO COMPLETE

I have explained the study (such as the purpose, risks, benefits and the procedures) to the study participant before the study participant voluntarily agreed to participate.

Name of Individual Conducting Informed Consent Discussion (print or type)

Signature of Individual Conducting Informed Consent Discussion

Date
(Individual Conducting Informed Consent Discussion must personally date)

FOR IMPARTIAL WITNESS TO COMPLETE

I witnessed that the information in the consent and any other written information was accurately explained to, and apparently understood by, the study participant, and that informed consent was freely given by the study participant.

Impartial Witness Name (print or type)

Signature of Impartial Witness

Date
(Impartial Witness must personally date)