

## READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

### PART III: PATIENT MEDICATION INFORMATION

#### ENTUZITY™ KwikPen® (insulin injection, human biosynthetic) Solution for Injection, 500 units/mL

www.lilly.ca



Read this carefully before you start taking ENTUZITY (In-Too-Za-Tee) and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about ENTUZITY.

#### **Serious Warnings and Precautions**

- Hypoglycemia (low blood sugar) is the most common side effect of insulin, including ENTUZITY. As with all insulins, the timing of low blood sugar may be different depending on the type of insulin you take.
- All patients with diabetes should check their blood sugar.
- High or low blood sugar that is not corrected can cause loss of consciousness, coma, or death.
- Do not use a syringe to remove ENTUZITY from your ENTUZITY KwikPen. The markings on a syringe will not measure your dose correctly. A severe overdose can happen, causing low blood sugar, which may put your life in danger.
- To reduce the chance of low blood sugar, do not inject ENTUZITY into a vein or muscle. Do not use ENTUZITY in an insulin pump, dilute ENTUZITY, or mix it with any other type of insulin or solution.
- Any change in insulin regimen, manufacturer, type, concentration, or how it is injected should be made carefully and only with your doctor's advice. Blood sugar should be checked more often when these types of changes are made.
- Only use ENTUZITY if it is clear and colourless.
- Errors have been reported with the use of concentrated insulins like ENTUZITY. Always check the label on your insulin before injecting your dose to be sure you have the correct medicine.

#### **What is ENTUZITY used for?**

- ENTUZITY is a synthetic human insulin that is used to control high blood sugar in patients with diabetes mellitus who need more than 200 units of insulin in a day.
- ENTUZITY contains 5 times as much insulin (500 units/mL) in 1 millilitre (mL) as synthetic human insulin (100 units/mL).
- It is not known if ENTUZITY is safe and effective in children or patients >75 years of age.
- ENTUZITY should not be used in combination with other insulins.
- ENTUZITY should not be used in an insulin pump.

**How does ENTUZITY work?**

Insulin is a hormone that decreases the amount of sugar in your blood and urine by increasing the uptake of sugar from your blood into various tissues, such as the liver, muscles, and fat.

When taken two times or three times per day as directed, ENTUZITY works as both a meal-time (fast-acting) and basal (long-acting) insulin.

**What are the ingredients in ENTUZITY?**

Medicinal ingredients: insulin injection, human biosynthetic

Non-medicinal ingredients: Glycerin, metacresol, zinc oxide, water for injection. (Sodium hydroxide and hydrochloric acid may be added during manufacture to adjust the pH.)

**ENTUZITY comes in the following dosage forms:**

ENTUZITY is a clear and colourless aqueous biosynthetic insulin solution for injection (500 units/mL) and is available in a 3 mL ENTUZITY KwikPen (prefilled, 1,500 units of insulin).

**Do not use ENTUZITY if:**

- You are having an episode of low blood sugar (hypoglycemia).
- You have an allergy to human insulin or any of the ingredients in ENTUZITY or components of the container.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ENTUZITY. Talk about any health conditions or problems you may have, including if you:**

- Have liver or kidney problems.
- Take other medicines, especially ones called TZDs (thiazolidinediones).
- Have heart failure or other heart problems. If you have heart failure, it may get worse if you take TZDs with ENTUZITY.
- Are pregnant, planning to become pregnant, or breast-feeding. It is not known if ENTUZITY will harm your unborn or breastfeeding baby.
- Have any endocrine disease such as: acromegaly (too much growth hormone), Cushing's syndrome (too much of the adrenal hormones or long-time use of cortisone-type drugs), hyperthyroidism (overactive thyroid gland), or pheochromocytoma (tumor of the adrenal gland).
- Have low potassium or are taking potassium lowering medication.
- Have an illness, especially with nausea and vomiting, diarrhea and/or fever because this may cause your insulin needs to change.
- Have trouble with your adrenal, pituitary or thyroid glands, because your doctor may decide to change your insulin dose
- Change your exercise routine, usual diet, or if you travel.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.

**Before you start using ENTUZITY, talk to your healthcare provider about low blood sugar and how to manage it.**

**Other warnings you should know about:**

- Do not share your ENTUZITY KwikPen with anyone, including family members, even if the needle on the delivery device has been changed. You may pass on a serious infection or get a serious infection from the other person.
- Do not operate heavy machinery, until you know how ENTUZITY affects you.
- Do not drink alcohol or use over-the-counter medicines that contain alcohol.
- Hypokalemia (low potassium) is a possible side effect with all insulins. You might be more at risk if you are on potassium-lowering drugs or losing potassium (e.g. diarrhea)
- Eye disorders: fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disorder
- Pain due to nerve damage: if your blood sugar level improves very fast, you may get nerve related pain; this is usually temporary
- Swelling around your joints: when you first start using ENTUZITY, your body may keep more water than it should. This causes swelling around your ankles and other joints. This is usually temporary.

**The following may interact with ENTUZITY:**

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

Some medicines can change your blood sugar level. This may mean your insulin dose has to change. So, before taking a medicine ask your doctor if it will affect your blood sugar and what action, if any, you need to take. You also need to be careful when you stop taking a medicine.

**If you take any of the medicines below, your blood sugar level may fall (hypoglycemia)**

- Other medicines for the treatment of diabetes
- Medicines used to treat high blood pressure and/or heart problems, such as: angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blocking (ARB) agents, disopyramide
- Fibrates (medicine used for lowering high levels of blood fats)
- Monoamine oxidase inhibitors (MAOI) (medicines used to treat depression)
- Medicines used to relieve pain and lower fever, such as pentoxifylline, propoxyphene and salicylates
- Sulfonamide antibiotics (medicines used to treat infections)
- Somatostatin analogs, such as octreotide
- Fluoxetine
- Anabolic steroids

**If you take any of the medicines below, your blood sugar level may rise (hyperglycemia)**

- Atypical antipsychotics (e.g., olanzapine and clozapine)
- Hormones, such as: estrogens and/or progesterone (alone or as contraceptive pills), somatropin, thyroid hormones, glucagon.
- Corticosteroids (used to treat inflammation)
- Danazol (medicine acting on ovulation)
- Protease inhibitors (used to treat HIV infection)
- Diuretics (also called water pills), used to treat high blood pressure or fluid retention
- Isoniazid (used to treat tuberculosis)

- Some medicines used to treat asthma, such as albuterol, epinephrine, terbutaline
- Niacin and phenothiazines
- Corticotropin
- Diphenylhydantoin

**If you take any of the medicines below, your blood sugar level may rise or fall**

- High blood pressure medicines, such as: beta-blockers or clonidine
- Some medicines used to treat mental health problems, such as: lithium salts.
- Octreotide and lanreotide (used to treat a rare condition involving too much growth hormone (acromegaly))
- Alcohol (including wine and beer)
- A medicine used to treat some parasitic infections, called pentamidine. This may cause too low blood sugar which is sometimes followed by too high blood sugar.

Some medicines may make it harder to recognize the warning signs of your blood sugar being too low (hypoglycemia). Such medicines include: beta-blockers medicines, clonidine, guanethidine, or reserpine.

Do not use insulin together with medicines used to treat type 2 diabetes belonging to a class called Thiazolidinediones (TZDs). The use of these medicines together may increase your risk of developing heart failure.

**How to take ENTUZITY:**

- Use ENTUZITY exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much ENTUZITY to use and when to use it.
- Know the amount of ENTUZITY you use. Do not change the amount of ENTUZITY you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- The ENTUZITY KwikPen is specially made to dial and deliver doses of ENTUZITY. Before injecting, select your dose based on the number of units shown in the dose window of the pen. Do not select your dose by counting the number of clicks. The pen is not recommended for use by the blind or visually impaired without the help of someone trained to use it.
- Do not use a syringe to remove ENTUZITY from your ENTUZITY KwikPen. The markings on a syringe will not measure your dose correctly. A severe overdose can happen, causing low blood sugar, which may put your life in danger.
- Use ENTUZITY two or three times a day 30 minutes before eating a meal. ENTUZITY is usually the only insulin that you will need.
- Inject ENTUZITY under your skin (subcutaneously). Do not use ENTUZITY in an insulin pump or inject ENTUZITY into your vein (intravenously) or your muscle (intramuscularly).
- Do not mix ENTUZITY in the KwikPen with any other type of insulin or liquid medicine.
- Change (rotate) your injection site with each dose so that the same site is not used more than approximately once a month. Do not inject into pits (depressions), thickened skin or lumps.

- Check your blood sugar levels. Ask your healthcare provider what your blood sugar levels should be and when you should check your blood sugar levels.
- Keep ENTUZITY and all medicines out of reach of children.
- Your dose of ENTUZITY may need to change because of a 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 or stop taking.
- Do not reuse needles. Re-using needles increases the chances of blocking your needle, which may cause incorrect dosing.
- **NEEDLES AND PENS MUST NOT BE SHARED** with anyone including family members. Never share an ENTUZITY KwikPen, even if the needle on the delivery device is changed. You may pass on a serious infection or get a serious infection from the other person.

**Overdose:**

If you have injected too much ENTUZITY, your blood sugar level may become too low (hypoglycemia). Check your blood sugar frequently. If your blood sugar gets too low, immediately take action to increase your blood sugar level. See “Get emergency medical help if you have:” below for more information.

If you have injected too much ENTUZITY, your potassium may become too low (hypokalemia). Hypokalemia must be corrected by a healthcare professional.

If you think you have taken too much ENTUZITY, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

**Missed Dose:**

If you have missed a dose of ENTUZITY or if you have not injected enough insulin, your blood sugar level may become too high (hyperglycemia). Check your blood sugar frequently. For information on the treatment of hyperglycemia, see Hyperglycemia section below.

Do not take a double dose to make up for a missed dose.

**What are possible side effects from using ENTUZITY?**

These are not all the possible side effects you may feel when taking ENTUZITY. If you experience any side effects not listed here, contact your healthcare professional. Please also see Serious Warnings and Precautions.

The following side effects may be observed while taking ENTUZITY:

- hypoglycemia (see Hypoglycemia section below).
- hyperglycemia (see Hyperglycemia section below).
- skin changes and reactions at the injection site (see Injection Site Reactions section below).
- allergic reactions (see Allergic Reactions section below).

## **Hypoglycemia (low blood sugar level)**

Hypoglycemia is one of the most frequent adverse events experienced by insulin users.

Insulin reaction (too little sugar in the blood, also called "hypoglycemia") can be brought about by:

- Taking too much insulin.
- Missing or delaying meals.
- Exercising or working too hard just before a meal.
- An infection or illness (especially with diarrhea or vomiting).
- A change in the body's need for insulin.
- A new insulin type, dose or schedule

If a usual meal cannot be obtained at the appropriate time, then to avoid hypoglycemia, you should take the amount of carbohydrate prescribed for this meal in the form of orange juice, syrup, candy, or bread and milk, without changing your insulin dosage. If it becomes necessary to omit a meal due to nausea and vomiting, you should test your blood sugar level and notify your doctor.

The first symptoms of insulin reaction usually come on suddenly and may include vague symptoms of fatigue, nervousness or “shakiness”, rapid heartbeat, nausea, and a cold sweat. It is of utmost importance that you understand that these symptoms demand immediate attention. Severe hypoglycemia may happen up to 24 hours after your injection of ENTUZITY.

Your ability to concentrate and to react may be impaired as a result of hypoglycemia. This may constitute a risk in situations where these abilities are of special importance (e.g., driving a car or operating machinery – see Serious Warnings and Precautions).

A few patients who experienced hypoglycemic reactions after being transferred to human insulin, such as ENTUZITY, have reported that these early warning symptoms were less pronounced than they were with animal-source insulin. Some people may not recognize when their blood sugar drops low (especially patients who have had diabetes for a long time, have diabetic nerve disease, whose blood sugar level improves quickly, who have switched from other insulin products, who experience recurring hypoglycemia, who have psychiatric illness, who are elderly, or who are using certain other medications).

Eating sugar or a sugar-sweetened product will often correct the condition and prevent more serious symptoms. Artificial sweeteners are not useful for the treatment of hypoglycemia.

If a person with diabetes becomes delirious or mentally confused, or suffers from loss of memory or delusions, diluted corn syrup or orange juice with sugar should be administered by mouth. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious should be treated with intravenous administration of glucose at a medical facility or should be given an injection of glucagon (either intramuscular or subcutaneous). The patient should be given oral carbohydrates as soon as consciousness is recovered. In the event of a hypoglycemic reaction, whether mild or severe, you should notify your doctor promptly so that any desirable change in diet or dosage can be determined.

## **Hyperglycemia**

Hyperglycemia (too much glucose in the blood) may develop if your body has too little insulin.

Hyperglycemia can be brought about by:

- changes in your health (illness, stress, or emotional disturbances).
- not taking your insulin or taking less than recommended by your health care professional.
- malfunction and/or misuse of the KwikPen.
- eating significantly more than your meal plan suggests.
- a new insulin type, dose, or schedule.
- some new medications, including prescriptions, over-the counter medication, herbs, vitamins and street drugs.

Symptoms of hyperglycemia include:

- confusion or drowsiness.
- increased thirst.
- decreased appetite, nausea, or vomiting.
- rapid heart rate.
- increased urination and dehydration (too little fluid in your body).
- blurred vision.
- flushed dry skin.
- acetone (fruity) odor of breath.

Hyperglycemia can be mild or severe. **It can progress to high glucose levels, diabetic ketoacidosis (DKA), and result in unconsciousness and death.**

### **What to do if you experience hyperglycemia**

- Test your blood sugar level and your urine for ketones as soon as you notice any of the above signs.
- Contact your doctor straight away if you have severe hyperglycemia or ketoacidosis.

### **Diabetic ketoacidosis (DKA)**

The first symptoms of diabetic ketoacidosis usually come on over a period of hours or days. With ketoacidosis, urine tests show large amounts of glucose and ketones.

Symptoms of diabetic ketoacidosis include:

First symptoms:

- drowsiness.
- flushed face.
- thirst.
- loss of appetite.
- fruity smelling breath.
- rapid, deep breathing.
- abdominal (stomach area) pain.

Severe symptoms:

- heavy breathing.
- rapid pulse.

Prolonged hyperglycemia or diabetic ketoacidosis can lead to:

- nausea.
- vomiting.
- dehydration.
- loss of consciousness.
- death.

**Severe or continuing hyperglycemia or DKA requires prompt evaluation and treatment by your health professional.** ENTUZITY should not be used to treat DKA, and people treating you should be advised that you are taking a concentrated long-acting insulin and about your regimen.

### **Allergic reactions**

A patient may be allergic to an insulin product **including ENTUZITY**. Severe insulin allergies may be life-threatening. **If you have any signs or symptoms of severe allergic reactions, seek medical help immediately.**

Signs of **severe** allergy include:

- a rash all over your body.
- shortness of breath.
- wheezing (trouble breathing).
- a fast pulse.
- sweating.
- low blood pressure.

### **Injection site reactions**

Injecting insulin **including ENTUZITY** can cause the following reactions on the skin at the injection site:

- a little depression in the skin (lipoatrophy).
- skin thickening (lipohypertrophy).
- skin lumps (localized cutaneous amyloidosis).
- redness, pain, swelling, itching, hives, or inflammation at injection site.

You can reduce the chance of getting an injection site reaction if you change the injection site each time. If you have local injection site reactions, contact your health professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

### **Heart Failure**

Taking certain diabetes pills called thiazolidinediones or “TZDs” with ENTUZITY may cause or worsen heart failure in some people. This can happen even if you have never had heart failure or heart problems before.

Tell your healthcare provider if you have any new or worse symptoms of heart failure including:

- shortness of breath.
- swelling of your ankles or feet.
- sudden weight gain.

**Get emergency medical help if you have:**

- Severe hypoglycemia needing hospitalization or emergency room care, and be sure to tell the hospital staff the dose of ENTUZITY that your healthcare provider has prescribed for you.
- Trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

**The most common side effects of ENTUZITY include:**

- Low blood sugar (hypoglycemia), allergic reactions including reactions at your injection site, skin thickening or pits at the injection site (lipodystrophy), itching, and rash.

<b>Serious side effects and what to do about them</b>			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and/or get immediate medical help
	Only if severe	In all cases	
<b>Severe Hypoglycemia</b> Hypoglycemia symptoms: shakiness, sweating, impaired concentration, impaired reaction time.		✓	✓
<b>Serious Hypersensitivity Reactions</b> Hypersensitivity symptoms: itching in mouth, swelling of lips and/or tongue, shortness of breath, coughing, wheezing, and hives.		✓	✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

### **Reporting Side Effects**

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

#### **3 ways to report:**

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program

Health Canada, Address Locator 1908C  
Ottawa, ON  
K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### **Storage**

Protect from heat and light. Do not freeze. Do not use ENTUZITY after the expiration date printed on the label or if it has been frozen.

#### Not In-Use (Unopened) ENTUZITY KwikPen

Unopened containers should be stored refrigerated at 2°C to 8°C (36°F to 46°F) until time of use. Do not use if it has been frozen.

#### In-Use (Opened) ENTUZITY KwikPen

Do NOT store in-use pen devices refrigerated. Pen devices must be stored unrefrigerated at a maximum temperature of 30°C (86°F), and the pen must be discarded after 28 days, even if the pen still contains ENTUZITY. Once the container has been punctured, the chemical and physical stability for the drug product has been demonstrated for 28 days at a maximum temperature of 30°C (86°F).

Keep out of reach and sight of children.

#### **If you want more information about ENTUZITY:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website [www.lilly.ca](http://www.lilly.ca) or by calling 1-888-545-5972.

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For more information, please contact your healthcare professionals or pharmacist first, or Eli Lilly Canada at: 1-888-545-5972 or visit the website at [www.lilly.ca](http://www.lilly.ca)

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

This leaflet was prepared by: Eli Lilly Canada Inc.

You may need to read this package insert again. Please do not throw away until you have finished your medicine.

Approved: July 27, 2017

Revised: March 26, 2021

ENT-0004-CA-PM-20210326