



CHMP Recommends Approval of Lilly's New Fast-Acting Mealtime Insulin to Improve Glycemic Control in Adults with Diabetes

January 31, 2020

INDIANAPOLIS, Jan. 31, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for Lilly's new mealtime insulin for the treatment of adults with diabetes as part of a multiple daily injection regimen or delivered by an insulin pump. This novel, fast-acting formulation of insulin lispro is being evaluated for use in adults with type 1 and type 2 diabetes to reduce blood glucose.

This is the first regulatory step toward approval for this new insulin in Europe. The CHMP opinion is now referred for final action to the European Commission, which grants approval in the European Union. Lilly plans to market the medicine under the trade name Liumjev™ in the European Union, and the medicine has been referenced to date as URLi or LY900014 in scientific disclosures.

"Today's CHMP opinion brings us another step closer to providing adults with diabetes in Europe with a new treatment option to help manage their blood glucose levels, especially their blood glucose levels following meals," said Deirdre Ibsen, global development leader for insulins, Lilly. "Maximizing the amount of time spent in the target blood glucose range is a constant balancing act and daily challenge. Many people with diabetes struggle to keep their blood glucose in the target range following meals and may benefit from a mealtime insulin with a fast onset of action."

The positive opinion was based on clinical pharmacological studies in type 1 and type 2 diabetes and studies from the PRONTO clinical program. PRONTO-T1D and PRONTO-T2D were designed as phase 3 treat-to-target trials in which each arm is treated to achieve the same level of glycemic control, allowing comparisons in other important treatment effects, such as rates of hypoglycemia, post-meal glucose control and glucose time in range. Both studies met the primary endpoint of non-inferior A1C reduction from baseline compared to Humalog at 26 weeks, when URLi and Humalog were dosed at mealtime. Further, URLi demonstrated superior reduction in blood glucose spikes at both one hour and two hours after a test meal compared to Humalog.

Overall, URLi showed no significant difference in severe, nocturnal or overall hypoglycemia rates in study participants compared to Humalog, and the two insulins had similar safety and tolerability profiles across Phase 3 studies.

Data from a phase 1 clinical pharmacology study in people with type 1 diabetes also showed that URLi was absorbed significantly faster into the blood stream compared to Humalog, insulin aspart and fast-acting insulin aspart. The early blood glucose profile with the investigational insulin closely matched that of participants without diabetes.

"We developed URLi to provide a mealtime insulin option that more closely mirrors the way insulin works in people without diabetes," Ibsen said. "We look forward to bringing this new treatment option to those living with diabetes as soon as possible."

Lilly has submitted URLi for approval with regulatory authorities in the U.S. and Japan.

About the PRONTO studies

PRONTO-T1D and PRONTO-T2D were randomized, double-blind, controlled, treat-to-target comparisons of fast-acting insulin lispro and Humalog (insulin lispro), both in combination with either insulin glargine or insulin degludec in adults with type 1 and type 2 diabetes, respectively. The primary objective of each study, conducted in 1,222 and 673 participants, respectively, was to evaluate whether fast-acting insulin lispro is non-inferior to Humalog in reducing A1C from the baseline after 26 weeks of treatment. Key endpoints were adjusted for multiple testing, including the comparisons of one and two hour post-prandial glucose and A1C superiority.

U.S. PURPOSE and SAFETY SUMMARY

Important Facts About Humalog® (HU-ma-log) and Insulin Lispro Injection

- Humalog is also known as insulin lispro injection.
- Humalog and Insulin Lispro Injection are fast-acting insulins. They are used to control high blood sugar in adults and children with diabetes. They are available only with a prescription.
- Humalog comes in two strengths: U-100 (100 units per milliliter) and U-200 (200 units per milliliter). The Humalog U-200 prefilled pen contains **2 times as much insulin** per 1 milliliter as standard (U-100) insulin. The dose window on the pen shows your insulin dose.
- It is not known if Humalog or Insulin Lispro Injection are safe and effective for children with type 2 diabetes or for children younger than 3 years of age with type 1 diabetes. There were no studies done with these insulins in these groups of children. If your doctor decides to give your child one of these insulins, he or she may give you special instructions.

All Humalog and Insulin Lispro Injection products contain insulin lispro.

Warnings

Do not take Humalog or Insulin Lispro Injection if you have:

- symptoms of low blood sugar (hypoglycemia)
- an allergy to insulin lispro products or any of their ingredients.

Do not reuse needles or share your insulin injection supplies with other people. This includes your:

- prefilled pen for use by a single patient
- cartridges
- reusable pen that works with Lilly 3mL cartridges
- needles
- syringes

You or the other person can get a serious infection. This can happen even if you change the needle.

Do not change the type of insulin you take or your dose, unless your doctor tells you to. This could cause low or high blood sugar, which could be serious.

Do not use a syringe to remove Humalog from your prefilled pen. This can cause you to take too much insulin. Taking too much insulin can lead to severe low blood sugar. This may result in seizures or death.

Humalog and Insulin Lispro Injection may cause serious side effects. Some of these can lead to death. The possible serious side effects are:

- **Low blood sugar.** This can cause:

- dizziness or light-headedness
- headache
- shakiness
- irritability
- sweating
- blurred vision
- fast heartbeat
- mood change
- confusion
- slurred speech
- anxiety
- hunger

If you are at risk of having severely low blood sugar, your doctor may prescribe a glucagon emergency kit. These are used when your blood sugar becomes too low and you are unable to take sugar by mouth. Glucagon helps your body release sugar into your bloodstream.

- **Severe allergic reaction.**

Get emergency help right away if you have:

- a rash over your whole body
- sweating
- extreme drowsiness
- swelling of your face, tongue, or throat
- trouble breathing
- a faint feeling
- dizziness
- a fast heartbeat
- shortness of breath
- confusion

- **Low potassium in your blood.** This can lead to severe breathing problems, irregular heartbeat, and death.

- **Heart failure.** Taking diabetes pills called thiazolidinediones (thIE-uh-zOH-li-dEEen-dIE-OHns), or "TZDs," with insulin lispro products may cause heart failure in some people. This includes people who do not have any heart problems. If you have heart failure, it may get worse if you take TZDs with these insulin lispro products. Tell your doctor if you have any new symptoms of heart failure, or if they get worse. Some symptoms of heart failure include: shortness of breath, swelling of ankles and feet, and sudden weight gain. Your doctor may need to change or stop treatment with TZDs and your insulin lispro product.

- **High blood sugar and ketoacidosis.** You can have these serious problems when your insulin pump or infusion set stops working. They can also happen if your insulin is no longer effective. For these reasons, always keep extra insulin injection supplies with you.

Common side effects

The most common side effects of **Humalog and Insulin Lispro Injection**, are:

- low blood sugar
- reactions where you have injected insulin
- swelling of your hands or feet
- itching
- allergic reactions
- changes in fat tissue where you have injected insulin
- weight gain
- rash

These are not all of the possible side effects. Tell your doctor if you have any side effects. You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch.

Before using

Talk with your doctor about low blood sugar and how to manage it. Also tell your doctor:

- about all of the medicines you take, including over-the-counter medicines, vitamins, and herbal supplements.
- about any other prescription medicines you take, especially ones called TZDs.
- about all of your medical conditions, including if you have heart failure or other heart, liver, or kidney problems.
- if you are pregnant, breastfeeding, or plan to become pregnant or breastfeed.

How to take

Read the **Instructions for Use** that come with your **Humalog or Insulin Lispro Injection**. Be sure to take your insulin lispro product and **check your blood sugar levels** exactly as your doctor tells you to. Your doctor may tell you to change your dose because of illness, increased stress, or changes in your weight, diet, or physical activity level. He or she may also tell you to change the amount or time of your dose because of other medicines or different types of insulin you take.

Before injecting your insulin lispro product

You can inject your insulin dose yourself, or you can have a trained caregiver inject it for you. Make sure you or your caregiver:

- Check the insulin label before each injection. This will help you make sure that you are taking the correct insulin.
- Use a new needle for each injection. You can get a serious infection or the wrong dose of insulin if you re-use needles.
- Change (rotate) where you inject your insulin with each dose. This can reduce your chance of getting pits, lumps, or thickened skin where you inject your insulin. **Do not** inject your insulin into the exact same spot or where the skin has pits or lumps. **Avoid** injecting into thickened, tender, bruised, scaly, hard, scarred, or damaged skin.

When you are ready to inject

- Inject Humalog or Insulin Lispro Injection, inject it under your skin within 15 minutes before or right after you eat a meal.

Staying safe while taking your insulin lispro product

To stay safe while taking your insulin, be sure to **never** inject Humalog U-200 in your vein, muscle, or with an insulin pump. Also be sure **not to**:

- mix Humalog U-200 with other insulins or liquids.
- drive or use heavy machinery until you know how your insulin lispro product affects you.
- drink alcohol or use other medicines that contain alcohol when taking your insulin lispro product.

Learn more

For more information, call 1-800-545-5979 or go to www.humalog.com or www.lillyinsulinlispro.com.

This summary provides basic information about Humalog and Insulin Lispro Injection. It does not include all information known about these medicines. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your doctor. Be sure to talk to your doctor or other health care provider about your insulin lispro product and how to take it. Your doctor is the best person to help you decide if these medicines are right for you.

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About Diabetes

An estimated 463 million adults worldwide have type 1 and type 2 diabetes.¹ Type 2 diabetes is the most common type.² Diabetes is a chronic disease that occurs when the body does not properly produce or use the hormone insulin.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research, collaboration and quality manufacturing, we strive to make life better for people affected by diabetes. We offer a wide range of therapies and a continued determination to provide real solutions – from medicines and technologies to support programs and more. For the latest updates, visit www.lillydiabetes.com.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/newsroom. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Lilly's fast-acting insulin lispro as a potential treatment of diabetes, and reflects Lilly's current beliefs. However, as with any pharmaceutical product or medical device, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there is no guarantee that the European Commission will approve Lilly's fast-acting insulin lispro based on the CHMP opinion, that, if approved, the fast-acting insulin lispro will be commercially successful, or that the company will meet its anticipated timelines for the roll out of this medicine. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to

reflect events after the date of this release.

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References

1. International Diabetes Federation. *IDF Diabetes Atlas, 9th edn*. Brussels, Belgium: 2019. Available at: <http://www.diabetesatlas.org>.
2. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Available at: <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>. November 2017.

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The Lilly logo is rendered in a vibrant red, cursive script. The letters are fluid and interconnected, with a prominent 'L' at the beginning and a long, sweeping tail on the 'y'.

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