



First-ever Study of Lilly's Humulin® R U-500 Administered in an Insulin Pump Shows Improved A1C in People with Type 2 Diabetes

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Study Results Evaluating Humulin R U-500 in Insulet Corporation's Omnipod® U-500™ Insulin Management System Presented at the American Diabetes Association 78th Scientific Sessions

INDIANAPOLIS, June 25, 2018 /PRNewswire/ -- Eli Lilly and Company's (NYSE: LLY) Humulin® R U-500 administered via an investigational insulin pump (Omnipod® U-500™ Insulin Management System) provided greater A1C reduction with less daily insulin needed compared to multiple daily injections (MDI) in adults with type 2 diabetes on high dose insulin (201-600 units/day).¹ Data from this phase 3 study will be presented for the first time today in an oral session at the American Diabetes Association (ADA) 78th Scientific Sessions® in Orlando. Humulin R U-500 is Lilly's highly concentrated insulin formulation that is used to control high blood sugar in people with diabetes who are insulin-resistant and need daily doses of more than 200 units of insulin.

"Concentrated insulins are effective treatment options for people with diabetes who have high insulin requirements," said Tom Hardy, senior medical director at Lilly. "People who prefer to use an insulin pump currently do not have an option specifically for Humulin R U-500, which is five-times concentrated. These data show that Humulin R U-500 delivered with this investigational pump may help people better manage their blood sugar levels."

At the study's primary endpoint of 26 weeks, Humulin R U-500 delivered in the investigational pump and through MDI led to A1C reductions from baseline in people with type 2 diabetes (-1.27 percent, -0.85 percent, respectively). Beginning at week eight through the duration of the study, A1C improvement was greater with the pump compared to MDI (-0.42 percent between treatment groups at the primary endpoint). Humulin R U-500 delivered in a pump also led to lower total daily insulin dose compared to MDI (difference of -0.47 units/kg at the primary endpoint).¹

There was no significant difference in documented symptomatic (≤ 70 mg/dL) or severe hypoglycemia between the pump (36.9 events/patient/year; 0.12 events/patient/year) and MDI (33.9 events/patient/year; 0.05 events/patients/year). Nocturnal hypoglycemia was higher with the pump (18.2 events/patient/year) compared to MDI (11.2 events/patient/year).¹

"These results show that Humulin R U-500 using Insulet Corporation's Omnipod technology may help make it easier for people to titrate to their individual needs and improve their blood glucose control," said Dr. Trang Ly, senior vice president and medical director, Insulet Corporation. "We look forward to continuing to work closely with Lilly on the development of the Omnipod U-500™ Insulin Management System and bringing this new innovation to market in the near future."

About the VIVID Study

The VIVID study was the first large, randomized, controlled study of Humulin R U-500 delivered in an insulin pump. It was an open-label, multicenter, parallel, randomized, controlled 26-week phase 3 interventional study in 420 people with type 2 diabetes on high dose insulin (201-600 units/day) with or without other diabetes medicines. The study evaluated the safety and efficacy of Humulin R U-500 delivered via Continuous Subcutaneous Insulin Infusion (CSII) to MDI. The primary objective of the study was to compare Humulin R U-500 delivered by CSII to MDI on A1C reduction from baseline.

Indication for Humulin® R U-500

- Humulin R U-500 is an insulin that is used to control high blood sugar in adults and children with diabetes mellitus who need more than 200 units of insulin in a day.
- Humulin R U-500 contains 5 times as much insulin in the same volume (500 units/mL) as standard insulin (100 units/mL).
- It is not known if Humulin R U-500 is safe and effective when used in combination with other insulins, when used in an insulin pump, or in children.

Important Safety Information for Humulin® R U-500

What is the most important information I should know about Humulin R U-500?

- Humulin R U-500 is highly concentrated and contains 5 times as much insulin in 1 mL as standard U-100 (100 units/mL) insulin.
- Do not share your Humulin R U-500 KwikPen or U-500 insulin syringes with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

Who should not take Humulin R U-500?

- Do not take Humulin R U-500 if your blood sugar is too low (hypoglycemia) or you are allergic to any of the ingredients in Humulin R U-500.

What should I tell my healthcare provider before taking Humulin R U-500?

- Tell your healthcare provider:
 - If you have liver, kidney, or heart problems or any other medical conditions.
 - If you are pregnant, plan to become pregnant, or are breast-feeding.
 - About all the medicines you take, including prescription (especially ones commonly called TZDs [thiazolidinediones]) and over the counter medicines, vitamins, and herbal supplements.
- **Before you start using Humulin R U-500, talk to your healthcare provider about low blood sugar and how to manage it.**

How should I use Humulin R U-500?

- Read the detailed Instructions for Use that come with your Humulin R U-500.
- Take Humulin R U-500 exactly as your healthcare provider tells you to. Your healthcare provider should show you how much Humulin R U-500 to use and when to use it.
- Know the dose of Humulin R U-500 you use. Do not change your dose 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.
- Humulin R U-500 KwikPen: The U-500 KwikPen is specially made to dial and deliver doses of Humulin R U-500 insulin. Do not use any syringe to remove Humulin R U-500 insulin from your U-500 KwikPen. The markings on certain syringes will not measure your dose correctly. A severe overdose can happen, causing low blood sugar, which may put your life in danger.
- Humulin R U-500 vial: There is a special U-500 insulin syringe to measure Humulin R U-500. Use only a U-500 insulin syringe to draw up and inject your Humulin R U-500. If you do not use the right syringe type, you may take the wrong dose of Humulin R U-500. This can cause you to have too low blood sugar (hypoglycemia) or too high blood sugar (hyperglycemia). Your healthcare provider should show you how to draw up Humulin R U-500.
- Use Humulin R U-500 30 minutes before eating a meal.
- Inject Humulin R U-500 under your skin (subcutaneously). Do not use Humulin R U-500 in an insulin pump or inject Humulin R U-500 into your vein (intravenously) or your muscle (intramuscularly).
- Do not mix Humulin R U-500 with any other type of insulin or liquid medicine.
- Change your injection site with each dose.
- Check your blood sugar levels. Ask your healthcare provider what your blood sugar level should be and when you should check your blood sugar.
- Your dose of Humulin R U-500 may need to change because of changes in your level of exercise, weight, or diet, or because of increased stress, illness, or other medicines you take.
- Keep Humulin R U-500 and all medicines out of the reach of children.

What should I avoid while taking Humulin R U-500?

- Do not drive or operate heavy machinery until you know how Humulin R U-500 affects you. Do not drink alcohol or use over-the-counter medicines that contain alcohol.

What are the possible side effects of Humulin R U-500?

- **Humulin R U-500 can cause serious side effects that can lead to death, including:**
 - **Low blood sugar.** Signs of low blood sugar may include dizziness or lightheadedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood changes, or hunger. Your healthcare provider may prescribe a glucagon emergency kit so that others can give you an injection if your blood sugar becomes too low (hypoglycemic) and you are unable to take sugar by mouth.
 - **Severe allergic reaction. Get medical help right away** if you have a rash over your whole body, have trouble breathing, a fast heartbeat, or sweating. These are signs of a severe allergic reaction.
 - **Low potassium in your blood.**
 - **Heart failure.** Taking certain diabetes pills called thiazolidinediones or "TZDs" with Humulin R U-500 may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure, it may get worse while you take TZDs with Humulin R U-500. Your healthcare provider should monitor you closely while you are taking TZDs with Humulin R U-500. 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, or sudden weight gain. Treatment with TZDs and Humulin R U-500 may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.

- **Get emergency medical help if you have:**
 - severe low blood sugar needing hospitalization or emergency room care. Be sure to tell the hospital staff the units of Humulin R U-500 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 Humulin R U-500 include** low blood sugar, allergic reactions including reactions at your injection site, skin thickening or pits at the injection site, itching, and rash.
- **These are not all of the possible side effects of Humulin R U-500.** Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How should I store Humulin R U-500?

- Keep away from heat and out of direct light. Do not freeze. Do not use Humulin R U-500 after the expiration date stamped on the label. Do not shake the vial.
- **Humulin R U-500 Vials:** Store unopened vials of Humulin R U-500 in a refrigerator. Store opened (in-use) vials of Humulin R U-500 in the refrigerator or at room temperature for up to 40 days. Throw away any opened vial after 40 days of use, even if there is insulin left in the vial.
- **Humulin R U-500 KwikPen:** Store unopened Humulin R U-500 KwikPens in a refrigerator. Store opened (in-use) Humulin R U-500 KwikPens at room temperature for up to 28 days. Do not refrigerate opened KwikPens. Throw away any opened KwikPen after 28 days of use, even if there is insulin left in the pen.

General Information about the safe and effective use of Humulin R U-500

- Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. **Do not** use Humulin R U-500 for a condition for which it was not prescribed. **Do not** give Humulin R U-500 to other people, even if they have the same symptoms you have. It may harm them.
- The Patient Information leaflet summarizes the most important information about Humulin R U-500. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Humulin R U-500 that is written for healthcare professionals. For more information go to www.humulin.com or call 1-800-545-5979.

Humulin R U-500 is available by prescription only.

For additional information, talk to your healthcare provider and please click to access [Full Prescribing Information](#), [Patient Information](#), and [Instructions for Use for vial and pen](#).

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About Diabetes

Approximately 30 million Americans² and an estimated 425 million adults worldwide have diabetes.³ Type 2 diabetes is the most common type internationally, accounting for an estimated 90 to 95 percent of all diabetes cases in the United States alone.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 <http://www.lillydiabetes.com/> or follow us on Twitter: [@LillyDiabetes](#) and Facebook: [LillyDiabetesUS](#).

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to 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 www.lilly.com and www.lilly.com/newsroom/social-channels.

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This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Humulin R U-500 delivered in an investigational insulin pump as a treatment for type 2 diabetes, and Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with study findings to date, that Humulin R U-500 will receive additional regulatory approvals or that Humulin R U-500 will prove to be commercially successful. 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. Grunberger, G., et al. Human Regular U-500 Insulin via Continuous Subcutaneous Insulin Infusion vs. Multiple Daily Injections in Adults with T2D: the VIVID Study – All Randomized Population. Abstract 351-OR. Presented at 78th American Diabetes Association Scientific Sessions; June 22-26, Orlando, FL.
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.
3. International Diabetes Federation. IDF Diabetes Atlas, 8th edn, 2017. Available at: <http://www.diabetesatlas.org/>. 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 classic, elegant feel. The 'L' is particularly large and prominent, leading into the 'i', 'l', 'l', 'e', and 'y' which follow in a similar flowing style. The overall appearance is that of a handwritten signature or a stylized brand mark.

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