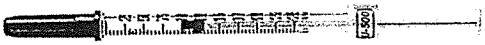
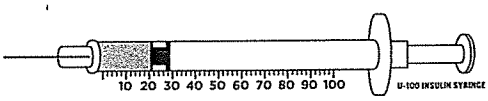
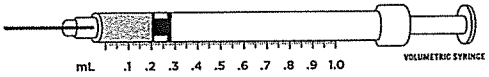
No dose conversion with Humulin® R U-500

Two ways to take U-500 insulin: U-500 KwikPen® or BD™ U-500 Insulin Syringe.
Dial or draw to the number of insulin units prescribed. No dose conversion needed.

DELIVERY METHOD		EXAMPLE: HOW TO DOSE 100 UNITS OF HUMULIN R U-500
CURRENT		
U-500 KwikPen		Dial to 100 No dose conversion: 100 units = 100 units
U-500 insulin syringe		Draw to 100 No dose conversion: 100 units = 100 units
OUTDATED CONVERSION INSTRUCTIONS	**DO NOT PRESCRIBE U-100 OR VOLUMETRIC SYRINGE OR INSTRUCT HOW TO USE WITH U-500 INSULIN**	
PREVIOUS		
U-100 insulin syringe		Draw to 20 Convert the dose: 100 units/5 = 20 unit mark
Volumetric syringe		Draw to 0.2 Convert the dose: 100 units/500 = 0.2 mL mark

CURRENTLY:
When the U-500 KwikPen or the U-500 syringe is used, no dose conversion is needed – a unit is a unit.

PREVIOUSLY:
When the U-500 vial was prescribed, the dose had to be converted for a U-100 insulin syringe or a volumetric syringe.

For more information, contact your Lilly representative, call The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979), or visit **Humulin.com/devices**

Indication for Humulin R U-500

- Humulin R U-500 is a concentrated human insulin indicated to improve glycemic control in adults and children with diabetes mellitus requiring more than 200 units of insulin per day.
- Limitation of Use: The safety and efficacy of Humulin R U-500 used in combination with other insulins has not been determined. The safety and efficacy of Humulin R U-500 delivered by continuous subcutaneous infusion has not been determined.

Select Safety Information for Humulin R U-500

- Instruct patients using the vial presentation to use only a U-500 insulin syringe and on how to correctly draw the prescribed dose of Humulin R U-500 into the U-500 insulin syringe. Confirm that the patient has understood these instructions and can correctly draw the prescribed dose of Humulin R U-500 with their syringe.

Select Safety Information for Humulin R U-500, continued

- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use). Train patients on proper use and injection technique before initiating Humulin R U-500. Training reduces the risk of administration errors such as needlesticks and dosing errors.
- Prescribe patients a U-500 insulin syringe to administer Humulin R U-500 from the vial to avoid administration errors. DO NOT use any other type of syringe.

Please see Important Safety Information on back and accompanying Full Prescribing Information. See Instructions for Use included with the pen and vial.

Lilly

Humulin® R U-500 KwikPen®
insulin human injection
500 units/mL

Important Safety Information for Humulin R U-500

Contraindications

- Humulin R U-500 is contraindicated during episodes of hypoglycemia and in patients hypersensitive to Humulin R U-500 or any of its excipients.

Warnings and Precautions

- **Dosing Errors: Extreme caution must be observed in measuring the dose of Humulin R U-500 because inadvertent overdose may result in serious adverse reaction or life-threatening hypoglycemia.**
- **Hyperglycemia, Hypoglycemia, or Death Due to Dosing Errors in the Vial Presentation:** Medication errors associated with the Humulin R U-500 vial resulting in patients experiencing hyperglycemia, hypoglycemia, or death have been reported.

  Dispensing
  - Instruct patients to always inspect insulin vials to confirm that the correct insulin is dispensed including the correct brand and concentration.
  - For the Humulin R U-500 vial, particular attention should be paid to the 20-mL vial size, prominent "U-500" and warning statements on the vial label, and distinctive coloring on the vial and carton.

  Prescribing
  - Dosing errors have occurred when Humulin R U-500 was administered with syringes other than a U-500 insulin syringe. Patients should be prescribed U-500 syringes for use with Humulin R U-500 vials. The dose of Humulin R U-500 should always be expressed in units of insulin.

  Administration
  - Instruct patients to always check the insulin label before each injection.
  - Use only a U-500 insulin syringe with Humulin R U-500 to avoid administration errors. Do not use any other type of syringe to administer Humulin R U-500. Adhere to administration instructions.
  - Instruct the patient to inform hospital or emergency department staff of the dose of Humulin R U-500 prescribed.
- If using the Humulin R U-500 KwikPen, patients should be counseled to dial and dose the prescribed number of units of insulin (NO dose conversion is required).
- DO NOT transfer Humulin R U-500 from the Humulin R U-500 KwikPen into any syringe for administration. Overdose and severe hypoglycemia can occur.
- **Never Share a KwikPen or U-500 Syringe Between Patients,** even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens.
- **Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen:** Changes in insulin, manufacturer, type, or method of administration should be made cautiously and only under medical supervision and the frequency of blood glucose monitoring should be increased.
- **Hypoglycemia:** Hypoglycemia is the most common adverse reaction associated with insulin, including Humulin R U-500. Severe hypoglycemia can cause seizures, may be life-threatening, or cause death. Severe hypoglycemia may develop as long as 18 to 24 hours after an injection of Humulin R U-500. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important, such as driving or operating other machinery.
  - Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual.
  - Early warning symptoms of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system, or in patients who experience recurrent hypoglycemia.
  - The timing of hypoglycemia usually reflects the time-action profile of the administered insulin formulation. As with all insulin preparations, the glucose lowering effect time course of Humulin R U-500 may vary in different individuals or at different times in the same individual and depends on many conditions.
  - Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.
- **Hypersensitivity and Allergic Reactions:** Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including Humulin R U-500. If hypersensitivity reactions occur, discontinue Humulin R U-500; treat per standard of care and monitor until symptoms and signs resolve.
- **Hypokalemia:** Insulin use can lead to hypokalemia that left untreated may cause respiratory paralysis, ventricular arrhythmia, and death. Use caution in patients who may be at risk for hypokalemia (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).
- **Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists:** Thiazolidinediones (TZDs), which are PPAR-gamma agonists, can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Observe patients for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

Warnings and Precautions, continued

Adverse Reactions

- Adverse reactions include hypoglycemia, allergic reactions, lipodystrophy, injection site reactions, weight gain, peripheral edema, and immunogenicity.

Drug Interactions

- Some medications may alter glucose metabolism and may necessitate insulin dose adjustment. Signs of hypoglycemia may be reduced or absent in patients taking antiadrenergic drugs. Particularly close monitoring may be required.

Use in Specific Populations

- **Pregnancy Category B:** While there are no adequate and well-controlled studies in pregnant women, evidence from published literature suggests that good glycemic control in patients with diabetes during pregnancy provides significant maternal and fetal benefits.
- **Pediatric Use:** There are no well-controlled studies of use of Humulin R U-500 in children. Standard precautions as applied to use of Humulin R U-500 in adults are appropriate for use in children.
- **Geriatric Use:** There are no well-controlled studies of use of Humulin R U-500 in geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemia.
- **Renal or Hepatic Impairment:** Frequent glucose monitoring and insulin dose reduction may be required in patients with renal or hepatic impairment.

Dosage and Administration

- Prescribe Humulin R U-500 ONLY to patients who require more than 200 units of insulin per day.
- Humulin R U-500 is available as a KwikPen or a multiple dose vial. Patients using the vial must be prescribed the U-500 insulin syringe to avoid medication errors.
- DO NOT perform dose conversion when using the Humulin R U-500 KwikPen. The dose window of the KwikPen shows the number of units of Humulin R U-500 to be injected and NO dose conversion is required.
- DO NOT perform dose conversion when using a U-500 insulin syringe. The markings on the syringe show the number of units of Humulin R U-500 to be injected. Each marking represents 5 units of insulin.
- Instruct patients using the vial to use only a U-500 insulin syringe and on how to correctly draw the prescribed dose into the syringe. Confirm that the patient has understood these instructions and can correctly draw the prescribed dose with their syringe.
- Advise the patient to read the Patient Information and Instructions for Use.
- Instruct patients to always check the insulin label before administration to confirm the correct insulin product is being used.
- Inspect Humulin R U-500 visually and only use if the solution appears clear and colorless.
- Administer Humulin R U-500 subcutaneously two or three times daily approximately 30 minutes before a meal. Rotate injection sites to reduce the risk of lipodystrophy.
- Individualize the dose of Humulin R U-500 based on metabolic needs, blood glucose monitoring results, and glycemic control goal.
- Do NOT administer Humulin R U-500 intravenously or intramuscularly.
- Do NOT mix Humulin R U-500 with other insulins.

Storage

- Protect from heat and light. Do not freeze. Do not use Humulin R U-500 after the expiration date stamped on the label.
- **Humulin R U-500 Vials:** Unopened vials of Humulin R U-500 should be kept in a refrigerator. Opened (in-use) vials of Humulin R U-500 should be kept in the refrigerator or at room temperature and used within 40 days of opening. Throw away any opened vial after 40 days of use, even if there is insulin left in the vial.
- **Humulin R U-500 KwikPen:** Unopened Humulin R U-500 KwikPens should be kept in a refrigerator. Opened (in-use) Humulin R U-500 KwikPens should be kept at room temperature and used within 28 days of opening. Do not refrigerate opened KwikPens. Throw away any opened KwikPen after 28 days of use, even if there is insulin left in the pen.

See accompanying Full Prescribing Information.
See Instructions for Use included with the pen and vial.

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Humulin® R U-500 KwikPen®

insulin human injection
500 units/mL

Lilly

Printed on post-consumer recycled paper.

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