Diabetes Educator Needed: Transitioning Inpatient Persons with Diabetes on U-500 Regular Insulin to Discharge Safely

Carol A. Biondi
MSN, RN, CDE
Diabetes Nurse Specialist
Tampa General Hospital
Tampa, FL

Renée M. Meehan
BSN, MA, RN, CDE
Diabetes Nurse Specialist
Tampa General Hospital
Tampa, FL

Disclosure to Participants
• Notice of Requirements For Successful Completion
  – Please refer to learning goals and objectives
  – Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
• Conflict of Interest (COI) and Financial Relationship Disclosures:
  – Presenter: Carol Biondi, RN, MSN, CDE – No COI/Financial Relationship to disclose
  – Presenter: Renée Meehan, RN, BSN, MA, CDE – Speaker’s Bureau: Eli Lilly Pharmaceuticals and Astra Zeneca
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  – Participants will be notified by speakers in any product used for a purpose other than for which it was approved by the Food and Drug Administration

Learning Objectives
• Identify differences between U-100 Insulins and U-500 Regular Insulin
• Describe pharmacology related to U-500 Regular Insulin
• Identify areas in which medication errors commonly occur and ways to prevent them
• Describe the role of the Diabetes Educator in the safe use of U-500 Regular Insulin as the patient transitions from hospital to home

What is U-500 Regular (U-500R) Insulin?
• Highly concentrated insulin
  – 500 units per mL
  – 5 times more concentrated than U-100 insulin
  – Enables administration of larger doses in smaller volumes
• Indication:
  – Severely insulin resistant patients requiring a TDD of U-100 insulin > 200 units (or > 150 units delivered by insulin pump - off label use)
• Potential for adverse drug events exists due to miscommunication of dosing and unfamiliarity with administration
  – Actual units
  – Unit markings
  – Volume
  – Pump units
Why Use U-500R Insulin?
- Reduced delivery volume
- Fewer total injections
- Cost effectiveness
- Increased patient satisfaction
- Improved glycemic control

Potential Candidates for U-500R Therapy
- Type 2 DM with obesity and/or severe insulin resistance
- Patients with insulin requirements > 200 units per day (or > 150 units delivered by insulin pump - off label use)
  - Post operative or post transplant state
  - High-dose glucocorticoid state
  - Severe systemic infection
- Gestational DM with severe insulin resistance
- Insulin resistant syndromes

U-500R Insulin: Clinical Pharmacology
- High concentration results in unique insulin pharmacokinetics resembling both basal and prandial activity
  - Onset: within 30 minutes
  - Peak effect: ~ 6 hours
  - Duration of action: up to 24 hours
  - Usually given 2-3 times daily 30 minutes before meals
- Time course action may vary in different individuals or at different times in the same individual
  - Blood flow at injection site
  - Sensitivity of insulin receptors

Comparison of U-500R and U-100R
- U-500R: slower absorption rate; longer duration; extended prandial and basal activity
- U-500R is Highly Concentrated
- U-500R contains 500 units in each milliliter (5 times more concentrated than U-100 insulin)
- Allows a patient to inject 1/5th the insulin volume when compared to injecting the same dose of a U-100 insulin

U-100R vs. U-500R Insulin
All syringes pictured here are displaying the same actual units (dose)
How to Measure 200 Actual Units?

A subcutaneous syringe has no markings. mL = 200 X Actual Units

A U-100 insulin syringe has Unit Markings. mL = 200 + Actual Units

U-100 Insulin Syringe vs Volumetric (TB) Syringe

U-100 Insulin Syringe
- Greater availability as outpatient
- Lower cost
- Needle length shorter (6mm)
- Smaller gauge (31g)

Volumetric (TB) Syringe
- Less availability as outpatient
- Higher cost
- Needle length longer (12.7mm)
- Larger gauge (27g)

U-500R: Dosage and Administration

- U-500R should only be administered subcutaneously
- U-500R takes effect within 30 minutes
- Patients should eat within 30 minutes of injection
- Most patients require 2-3 injections daily
- Mixing with other insulins is not recommended
- Use a U-100 insulin syringe or volumetric (TB) syringe
- Amount should be written in actual units and unit markings on a U-100 syringe or volume (mL) if using a volumetric (TB) syringe

Prescription Writing for U-500R

- Written based on type of syringe patient will use
  - U-100 Insulin syringe
  - Volumetric (TB) syringe
- Should provide both actual units of U-500R and amount to be administered indicated as respective markings on designated syringe
- Word CONCENTRATED should be added to the prescription

Examples of Prescription Writing

- Example using U-100 insulin syringe
  - Human Regular (CONCENTRATED) U-500 Insulin sig: 150 actual units subcutaneous twice daily 30 minutes before meals - breakfast and supper - draw to 30 unit markings on U-100 insulin syringe
- Example using volumetric (TB) syringe
  - Human Regular (CONCENTRATED) U-500 Insulin sig: 150 actual units subcutaneous twice daily 30 minutes before meals - breakfast and supper - draw to 0.3 mL on volumetric syringe

Algorithm for U-500 Regular Insulin
Conversion from U-100 to U-500R

Dosing should be consistent with previous insulin TDD and titrated according to A1C
- **Baseline A1C between 8% - 10%**
  - Dose for dose conversion
- **Baseline A1C ≤ 8%**
  - Consider reducing U-500R by 10% – 20%
- **Baseline A1C ≥ 10%**
  - Consider increasing U-500R by 10% - 20%

Patient Case Study

- Maria has been on insulin therapy for 10 years. BG are 120 – 200 mg/dL. Her A1c is 8%. Her current regimen includes:
  - Lantus 62 units BID
  - Novolog 42 units TID with meals
  - Total daily insulin dose: 250 units daily
- Does Maria qualify for U-500R insulin? **YES!**
  - Dosing strategy: 125 actual units U-500R BID 30 minutes before breakfast and supper
  - 125 actual units U-500R = 25 unit markings on a U-100 insulin syringe

Titrating Doses Further

- Twice daily doses before breakfast and supper
  - To adjust morning dose use blood glucose readings before lunch and supper
  - To adjust supper dose use blood glucose readings at bedtime, overnight, and fasting the next morning
- Three times per day before meals
  - To adjust morning dose use blood glucose readings before lunch
  - To adjust lunch dose use blood glucose readings from supper
  - To adjust supper dose use blood glucose readings at bedtime, overnight, and fasting the next morning

U-500R in Insulin Pumps – Off Label Use

- May improve A1C in patients who require large doses of insulin
  - Lower volume needed
  - Reduced leakage at infusion site
  - Reduced pump cartridge change
  - Reduced infusion set change
  - Extended battery life

U-500R in Insulin Pumps – Off Label Use

- Current insulin pumps do not have software that can correct for delivery of U-500R
  - Programmed doses must be divided by 5 to obtain the TDD delivered in “pump units”
  - Insulin on board function should be entered for at least 6 hours
  - Bolus doses are recommended 30 minutes before a meal
Avoiding Medication Errors

- Confirm patient’s U-500R insulin dose by having the patient demonstrate on the same syringe they will use at home (insulin or volumetric)
- Use conversion chart to assist with ordering/administering U-500 insulin
- Express dose in actual units of U-500 insulin along with unit markings or volume depending on the syringe the patient uses at home
  - U-100 insulin syringe
  - Volumetric (TB) syringe

U-500R: Safety Considerations

- Extreme caution must be observed in measurement of U-500R because inadvertent overdose may result
- Hypoglycemia is the most common adverse reaction of all insulin therapies
- Severe hypoglycemia may develop 18-24 hours after the original injection of U-500R
- Frequent glucose monitoring is recommended
- Significant others should be instructed on the appropriate use of glucagon

U-500R: Labeling

- U-500R insulin is distinctively labeled to differentiate it from U-100R insulin
  - Carton and vial label are marked with diagonal brown stripes and name is in bold red letters
  - Carton has statement in bold, red letter: “Warning-High Potency Not for Ordinary Use”
  - Vial contains 20 mL (10,000 units) vs the U-100 vial, which contains 10 mL (1000 units)

Conversion Chart

<table>
<thead>
<tr>
<th>U-500R U-500 units</th>
<th>U-100 insulin syringe (with syringe guide)</th>
<th>Tuberculin syringe (volume in mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>20 mL (1000 units)</td>
<td>0.5 mL</td>
</tr>
<tr>
<td>15</td>
<td>15 mL (750 units)</td>
<td>0.75 mL</td>
</tr>
<tr>
<td>10</td>
<td>10 mL (500 units)</td>
<td>1.0 mL</td>
</tr>
<tr>
<td>5</td>
<td>5 mL (250 units)</td>
<td>1.5 mL</td>
</tr>
<tr>
<td>2.5</td>
<td>2.5 mL (125 units)</td>
<td>3.0 mL</td>
</tr>
<tr>
<td>1</td>
<td>1 mL (50 units)</td>
<td>4.0 mL</td>
</tr>
</tbody>
</table>

Vial/Box Appearance U-500R vs U-100R

- A 20 mL U-500R vial contains 10x more insulin units than a 10 mL U-100 vial
U-500R: Storage
• Unopened: Vials not in use should be stored in refrigerator (36º-46ºF)
• Opened: Vials currently in use can be kept unrefrigerated at room temperature (below 86ºF)
• In-use vials must be used within 40 days or be discarded, even if they still contain insulin

U-500R: Stability in Prefilled Syringes
• Prefilled syringes are stable for at least 28 days when stored under refrigeration
• Prefilled syringes may be used for patients who are unable to accurately draw up their own doses

Inpatient Use of U-500R
• Home dosage must be verified by designated professional (nurse, pharmacist, or CDE) through patient demonstration using the type of syringe used at home
• Diabetes Educator should be consulted on admission and continue to follow patient in preparation for discharge
• Orders must be written with dosage in actual units and volume or unit markings depending on type of syringe to be used
• “High Alert Medication” labeling in the EMR & on the actual product advised
  – Word CONCENTRATED should precede U-500R name
  – U-500R should be separate from U-100 insulins in EMR

Inpatient Use of U-500R
• Store, dispense, and administer separately from U-100 insulins to reduce administration errors
  – Pharmacist may prepare each individual dose in a specified syringe
  – Vial may be sent to the floor for nurse preparation (with dual confirmation)
• Frequent blood glucose assessment at least 4 times daily (usually before meals and at bedtime) in consideration nocturnal blood glucose checks
• Notify physician immediately for hypoglycemia and provide prompt treatment according to hospital protocol
• Adjust U-500R dosage as appropriate
• For discharge, prescriptions should be entered as actual dosage and volume or unit markings depending on the type of syringe to be used and transmitted to the pharmacy

Tampa General Hospital
• 1,018 Beds
• Level 1 Trauma Center
• Magnet Recognition
• Specialties
  – Critical Care
  – Neurology & Stroke Center
  – Burn Center
  – Cardiology
  – Cardiology
  – Cardiothoracic
  – Urology
  – Nephrology
  – Urology
  – Endocrinology
  – GI
  – Diabetes & Endocrinology
  – Children’s Center
  – Genetics
Inpatient Use of U-500R at Tampa General Hospital

- Ensure patient's required daily dose exceeds 200 actual units insulin (to assess for appropriateness of U-500 use)
- Ensure other orders for basal-bolus insulin have been discontinued
- Rationale that U-500 insulin is regular insulin in a 5-times concentrated form when communicating with patient and caregivers
- U-500R ordered in the EPIC EMR system
- Patient's nurse notifies Pharmacy 1 hour prior to ordered dose time
- Prepared in Pharmacy IV room
- Checked by 2 pharmacists
  - First check: IV room pharmacist
  - Second check: Supervisor against PTA list
- Hand delivered to Patient's Nurse
  - Double check by Nurse/Nurse or Nurse/Pharmacist
  - Final check Nurse/Patient

Ordering U-500R in Epic

- U-500 ordering panel:
Inpatient Precautions

- Hypoglycemia
  - Hypoglycemia is the most common adverse reaction with all insulin therapies and can be deadly in accidental overdoses.
  - Severe hypoglycemia may develop 18-24 hrs after original injection.
  - Must be assessed and treated promptly.
- Hyperglycemia
  - Under-dosing is common.
  - Frequently occurs in the hospital setting.
    - Providers are reluctant to prescribe U-500.
    - Unit markings are mistaken for the number of actual units.
    - U-100 insulin is ordered by mistake.

Diabetes Educator Role With U-500R

- Reconcile correct dose of U-500R on admission.
- Educate nursing, pharmacy and providers.
- Educate the patient:
  - Accurate communication of dosage.
  - Identify correct markings on designated syringe.
  - Identification of U-500R package.
  - Identify and treat hypoglycemia.
- Ensure that take-home instructions and prescriptions are accurate and clear.

Diabetes Education Department

On The Horizon
New Insulin Formulations

- Glargine U-300
- Lispro U-200
- Degludec
- PEGylated Lispro

*Not FDA Approved

Novel Insulin Product

- U-300 Insulin (Toujeo)
  - Variation of insulin glargine (Lantus).
  - Studied in the EDITION trials.
  - Concentration = 300 units/mL.
  - Potentially less hypoglycemia than Lantus.

Pharmacokinetics of U-300 Insulin Glargine in Healthy Volunteers

- U-100 0.4 U/kg (n = 24)
- U-300 0.4 U/kg (n = 23)

Source:
Glargine U-300 (Toujeo)

- FDA approved in February 2015
- Prefilled pen contains 450 units
- U-300 insulin glargine offers a smaller depot surface area leading to a slower rate of absorption
- Provides flatter and prolonged pharmacokinetic and pharmacodynamic profiles and more consistency
- Half-life is ~23 hours
- Steady state achieved in 5 days
- Duration of action ≤36 hours

Lispro U-200 (Humalog U-200)

- FDA approved in May 2015
- Pre-filled pen contains 600 units
- Concentration = 200 units/mL
- Lasts longer between pen changes
- Maximum of 60 units per injection

What's Next?

U-100
U-40
U-200
U-300
U-500

References

- Collier, I. Practical pearls for the management of patients on U-500 regular human insulin. AADExpo 2015.
- U-500 Regular Insulin prescribing statements. Indianapolis, IN: Eli Lilly and Company; 2014.