Addressing safety concerns about U-500 insulin in a hospital setting

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Purpose. Safety precautions for the use of U-500 insulin in a hospital setting are described.

Summary. St. Vincent Indianapolis Hospital, a 500-bed community hospital, formed a committee to develop a U-500 insulin policy to address the unique considerations required for this drug at all steps of the medication management process. An order set was designed by the multidisciplinary team to standardize prescribing and ensure safety measures are consistently applied. Home dose verification by a pharmacist or certified diabetes educator is required to avoid inaccurate dosing. U-500 insulin is not stocked or stored in the automated dispensing machines on the nursing unit. When an order for U-500 insulin is received, a two-pharmacist order-entry process unique to this drug is followed. The total dose in units is entered, and the computer converts the dose to volume. A pharmacist checklist and dispensing kit are stored with the product to ensure that all safety precautions have been completed. A pharmacist hand delivers the insulin to the charge nurse and bedside nurse, at which time a safety time-out is taken to review the key characteristics of the drug, the physician order, and the medication administration record. Tuberculin syringes are used to administer U-500 insulin, and patients are taught how to use this syringe. Staff members also receive education regarding the U-500 insulin policy and procedure.

Conclusion. Safety precautions for hospital use of U-500 insulin employed a multilayered, multidisciplinary process using safeguards at every step in the medication management process.

Index terms: Concentration; Dispensing; Dosage; Drug administration; Education; Health professions; Hospitals; Insulin; Insulins; Pharmaceutical services; Pharmacists, hospital; Pharmacy, institutional, hospital; Prescribing; Protocols; Syringes; Team; Toxicity

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U-500 regular insulin has been used since the 1950s to treat diabetic patients with severe insulin resistance.[1,2] It is five times more concentrated than U-100 regular insulin (500 units/mL versus 100 units/mL).[3] Both products have an onset of action of 30 minutes; however, due to the concentration, U-500 insulin is regarded as having a more consistent rate of absorption, resulting in a prolonged duration of action lasting up to 24 hours.[1-5] Due to this pharmacokinetic difference, U-500 insulin is not interchangeable on a unit-to-unit ratio with U-100 insulin.[1,2]

Severe insulin resistance has been traditionally associated with "other" forms of diabetes mellitus, specifically acquired forms of lipodystrophy, insulin receptor defects, gestational diabetes with severe insulin resistance, and insulin receptor autoantibodies.[1,2,4-6] U-500 insulin is ideal for patients with severe insulin resistance because large doses of insulin (greater than 100 units) can be administered with fewer injections and because the formulation is associated with cost savings on insulin (unit per unit) and insulin supplies.[1,2,4-6]

Health care professionals today are faced with a new type of patient with severe insulin resistance. Some patients with morbid obesity and type 2 diabetes are responding to U-500 insulin therapy when traditional insulin therapies have failed to achieve the desired outcomes.[1,2,4] Lane, Cochran, and colleagues[1,2] defined severe insulin resistance as requiring over 200 units of insulin per day or an insulin dose of more than 2 units/kg/day. Based on their successful research involving this pa-

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tient population, they have published U-500 dosing recommendations.[1,2,4,5] With the positive outcomes of this research and publication of dosing recommendations, the use of U-500 insulin is expected to increase. Hospitals and other treatment facilities need to prepare for patients requiring U-500 insulin therapy.

Policy and procedure development

The American Society of Health-System Pharmacists and the Institute for Safe Medication Practices (ISMP) recommend that each organization specifically define circumstances in which U-500 insulin may be used.[7,8] In March 2009, a multidisciplinary team was formed at our 500-bed community hospital to develop a U-500 insulin policy to address the unique considerations required at all steps of the medication management process: prescribing, storage, dispensing, administering, and monitoring. In addition, the team addressed staff education to support the safe-use initiatives. When U-500 insulin is identified as a home medication or on a physician's order, the U-500 concentrated insulin policy and procedures are activated. Initiation or alteration of U-500 insulin is limited to specialists in endocrinology, but all credentialed prescribers may order U-500 insulin for continuation of outpatient diabetes management.

Prescribing. An order set was designed by the multidisciplinary team to standardize prescribing and ensure safety measures are consistently applied (Figure 1). Perhaps the most challenging aspect of prescribing U-500 insulin relates to the lack of a U-500 calibrated syringe. Patients are required to measure their dose in "unit markings" on a U-100 insulin syringe or milliliters (volume) on a tuberculin syringe. To prevent inaccurate dosing and reduce confusion, an essential component of medication reconciliation is verification of the patient-reported home dose of U-500 insulin.[1]

Home dose verification by a pharmacist or certified diabetes educator (CDE) is necessary before ordering U-500 insulin. During the verification process, patients select the syringe they use at home: an insulin syringe or a tuberculin syringe. Patients are asked to demonstrate how they measure their insulin for each dose. The verifier confirms each measurement, determines the actual units administered, and documents this information on the verification section of the order set for U-500 insulin. Once verification is complete, the prescriber writes the orders for U-500 insulin on the U-500 insulin order set, and doses are expressed in actual units and volume, as recommended by ISMP.[1,8,9] During the verification process, the pharmacist or CDE explains the importance of home dose verification to patients and highlights the differences between U-500 insulin and standard insulins. Patients are introduced to the phrase "units measured on an insulin syringe," and the CDE follows up with more in-depth patient education before discharge.

Storage. ISMP recommends that U-500 insulin be stored separately from other insulins to reduce dispensing errors.[10] In the pharmacy, U-500 insulin is stored separately from other insulins in the refrigerator designated for Schedule II controlled substances. The storage area is marked with physical alerts consistent with the organization's high-alert medication policy. U-500 insulin is not stocked or stored in the automated dispensing machines on the nursing unit. When the drug is needed for a specific patient, it is stored securely in the individual patient's medication storage area in accordance with the organization's high-alert medication measures. At patient discharge, the drug is immediately removed from the nursing unit for disposal.

Dispensing. Erroneous selection of U-500 insulin by physicians or pharmacists has been reported when U-500 insulin is listed on the inventory screen of computer systems,[10-12] possibly due to the incorrect assumption that there is only one concentration of insulin available. The risk of this error may be reduced by removing U-500 insulin from the browser, requiring the name to be typed in its entirety to locate the drug in the database.[10]

When an order for U-500 insulin is received, a two-pharmacist order-entry process unique to this drug is followed. The pharmacist entering the order manually types "U-500 insulin" in the database. The total dose in units is entered, and the computer converts the dose to volume. A second pharmacist reviews the order for the correct dose and volume before order activation.

Safety time-out. A pharmacist checklist (appendix) and dispensing kit containing information on the proper labeling, storage, and administration of and education about U-500 insulin is stored with the product and used by the pharmacist to ensure that all safety precautions have been completed. The patient label applied to the insulin vial is highlighted to differentiate the vial from other medications, and warning labels are affixed. A pharmacist hand delivers the insulin to the charge nurse and bedside nurse.

On arrival to the unit, a safety time-out is taken. The pharmacist who delivers the insulin, the charge nurse, and the bedside nurse review the key characteristics of the drug, the physician's order, and the medication administration record (MAR). Emphasis is placed on the dose (expressed in units and volume), the use of a tuberculin syringe with a safety needle, the storage and disposal procedures described on the MAR, and the warning labels. Written information reviewed and stored with the insulin includes U-500 drug information, dose

Figure 1. St. Vincent Health U-500 insulin order set.

03A PHYSICIAN ORDERS

St. Vincent Health

Allergies: *List Reaction:*

Patient ID

CHECK Applicable Orders

☐ **New Patient Start** (Skip Dose Verification section and see Physician Orders below-New starts restricted to Endocrinology)

Patient/care provider verbalized and demonstrated measuring to the marks described for each dose below:

Dose measured using an Insulin Syringe	Dose measured using a Tuberculin Syringe
Patient uses **INSULIN SYRINGE** at home (reports unit marking measured on an insulin syringe)	Patient uses **TUBERCULIN SYRINGE** at home (reports measuring dose in volume – mL)
☐ **Breakfast Dose:**	☐ **Breakfast Dose:**
5 X _____unit marking on an **INSULIN SYRINGE** = _____ units **U500 insulin** administered.	500 X _____mL = _____ units **U500 insulin** administered
☐ **Lunch Dose**:	☐ **Lunch Dose**:
5 X _____unit marking on an **INSULIN SYRINGE** = _____ units **U500 insulin** administered.	500 X _____mL = _____ units **U500 insulin** administered
☐ **Dinner Dose:**	☐ **Dinner Dose**:
5 X _____unit marking on an **INSULIN SYRINGE** = _____ units **U500 insulin** administered.	500 X _____mL = _____ units **U500 insulin** administered.
☐ **HS Dose:**	☐ **HS Dose:**
5 X _____unit marking on an **INSULIN SYRINGE** = _____ units **U500 insulin** administered.	500 X _____mL = _____ units **U500 insulin** administered.

☐ **Transfer medications**
- ☐ Doses confirmed as described above.
- ☐ Doses confirmed with previous institution and listed above. Unable to obtain demonstration.

Date:_____ **Time:**_____ _____ _____

Dose Verifier signature (RPh, Certified Diabetes Educator, or qualified licensed designee) Pager/Phone

PHYSICIAN ORDERS

[all **U500 insulin** must be delivered with a **tuberculin syringe**. Orders must be expressed in **total units** as well as **volume** (**mL**)]

☐ **Breakfast Dose** _____units **U500 insulin** ÷ 500 = _____mL **U500 insulin** SC 30 minutes prior to meal

☐ **Lunch Dose** _____units **U500 insulin** ÷ 500 = _____mL **U500 insulin** SC 30 minutes prior to meal

☐ **Dinner Dose** _____units **U500 insulin** ÷ 500 = _____mL **U500 insulin** SC 30 minutes prior to meal

☐ **Bedtime Dose** _____units **U500 insulin** ÷ 500 = _____mL **U500 insulin** SC 30 minutes prior to snack

Blood Glucose & Lab Testing :
- ☑ A1C test ☐ Fasting BMP on_____ ☐ Fasting lipid panel
- ☑ Eating or bolus tube feedings: Test BG before meals and at bedtime.
- ☐ Other tests _____

Call orders: Call results to LIP (Licensed Independent Practitioner)
- ☑ If BG falls below 70 twice within 24 hours or with severe hypoglycemic event
- ☑ Call for changes of the following: oral intake, bolus tube feedings, and/or steroid dose.
- ☑ If patient becomes NPO, discontinue U500 insulin and obtain order for insulin drip.
- ☐ Other tests _____

Diet: ☐ 1800 calorie diabetes meal plan ☐ Other _____

Consults: ☐ Endocrinologist_____
- ☑ Notify Unit Nursing Director or Charge Nurse of patient arrival now
- ☑ Consult Diabetes Nurse Educators (pager #3422): indication U500 insulin patient

Patient Education ☑ Verify patient's U500 insulin dose by demonstration and document on this form.
- ☑ Inform patient of use of tuberculin syringe during hospital stay.

Date:_____ **Time:**_____ _____ **M.D.** _____

Pager/Phone

21481 0909

USE BALL POINT PEN PRESS FIRMLY

Page 1 – MEDICAL RECORDS

CONCENTRATED U500 REGULAR INSULIN ORDER SET (ADULT)

conversion calculations (Figure 2), and policy and procedure highlights. The safety time-out is complete after warning labels are placed on the patient's medical and bedside charts and on the individual patient's secure medication storage area.

After the safety time-out, the charge nurse is responsible for acquiring any additional supplies needed (e.g., tuberculin syringe, safety needles) and contacting the unit nursing director and diabetes nurse educators. The nursing director is responsible for ensuring the continuity of nursing care for the patient and scheduling inservice education on U-500 insulin for charge nurses and nurses anticipated to care for the patient. The inservice education sessions are led by the CDE, a clinical pharmacist, or both. If the session does not occur before the nursing shift change, the bedside nurse is responsible for complete U-500 insulin handoff communication on to the next bedside nurse. The CDE and clinical pharmacist remain involved in the care of the patient throughout the patient's hospitalization.

Administration. ISMP recommends administering all U-500 doses in the hospital with a tuberculin syringe, regardless of the type of syringe the patient uses at home.[9] The team considered two approaches to ensure that the correct dose is administered. The first was to have the pharmacy dispense patient-specific doses. This option added another layer to the medication management process, resulting in additional risks for error, delays in care if doses were changed, and fewer educational opportunities on self-administration. The second option was to dispense the vial and allow the nurse or patient (under nursing supervision) to draw up the dose for administration. The latter option was chosen, and education materials were developed to ensure proper administration.

The tuberculin syringes used at our institution have a standard detachable needle. The nurses are instructed to remove that needle and replace it with a safety needle before drawing up the U-500 insulin dose. This step is essential, because there is approximately 0.07 mL of dead space between the detachable needle and the tip of the syringe. If the insulin is drawn before the safety needle is attached, approximately 35 units of U-500 insulin would not be administered. As with all insulins and high-alert medications, an independent double check by another health care professional must be performed and documented before the administration of each dose.[7,9] U-500 insulin is always administered subcutaneously, never intravenously.[3] To reduce the risk of hypoglycemia, the U-500 insulin policy advises against administering U-500 insulin to patients in the intensive care unit, who have orders to receive nothing by mouth, or for whom dose verification cannot be obtained. In these circumstances, an insulin infusion is recommended.

Staff awareness and education. U-100 is the most commonly used concentration of insulin, and health care professionals may be unaware of how it differs from U-500 insulin. After implementation of the U-500 insulin policy, basic information about U-500 insulin was provided to a variety of health care professionals via broad-reaching education to hospital staff—through grand rounds, continuing-education sessions, Web-based educational training, and in-service education sessions. Because time may lapse between patients receiving U-500 insulin, real-time education is crucial for patient safety. On receipt of a new order, CDEs, nursing directors, and pharmacists are deployed to provide information about U-500 regular insulin at the bedside. Written information provided at the safety time-out is often copied and distributed among the staff and inserted into the patient's charts for reference. Inservice education regarding U-500 insulin is provided to nursing staff on the unit within 24 hours of the patient's admission and repeated if requested.

One-year follow-up

Our hospital's multidisciplinary team met in April 2010 to review U-500 insulin experiences and identify areas for improvement. During the first year of policy implementation, 12 patients came to our institution with U-500 insulin as a home medication. In each case, individual circumstances not covered by the policy and procedure required clinical judgment. These included patients who underwent bariatric surgery, a disoriented patient unable to verify the home dose of insulin, U-500 insulin prescribed in the emergency department, and dietary changes while in the hospital that resulted in hypoglycemia. Despite the policy, U-500 insulin is prescribed infrequently, and awareness of this insulin continues to be a challenge. Pharmacists are heavily relied on to identify patients based on medication orders or medication reconciliation. Nursing associates were often unaware of their responsibilities after a patient using U-500 insulin was admitted and often did not notify the CDEs. At times, the order set led to confusion among physicians, nurses, and pharmacists and did not meet the needs of patients for whom a "corrective" U-500 insulin dosing schedule was prescribed.

A statement was included noting that there will be unique inpatient exceptions requiring deviation from the policy and procedure. These circumstances are handled and reviewed on a case-by-case basis by a physician, CDE, or clinical pharmacist to ensure that as many safeguards as possible remain intact. A recommendation was added to treat patients who are unable to verify their home U-500 insulin dose and bariatric surgery patients with an insulin infusion. U-500 insulin was determined not to be an emergent

Figure 2. Written information stored with the insulin and included in the patient's chart for reference. This document highlights U-500 insulin information and conversion calculations.

CAUTION

This Patient is receiving Regular Insulin U500

- To ensure patient safety, deliver Humulin R U500 insulin via a
  ** **TUBERCULIN SYRINGE ONLY** Given Sub-Q Route ONLY**
- Always use a safety needle when using the tuberculin syringe.
- **Warning:** Humulin R U500 insulin is a **concentrated** insulin.
  It contains 500 units per mL (it is **5 Xs the concentration** of other insulins).
- Physicians MUST write insulin orders in **units as well as volume (mL).**
- Below is a reference for converting units of insulin to volume (mL).
- **Always** do an **independent double check** when calculating and measuring insulin doses.

Units Insulin	Volume (mL) to be measured on Tuberculin Syringe ONLY
25	0.05
50	0.10
75	0.15
100	0.20
125	0.25
150	0.30
175	0.35
200	0.40
225	0.45
250	0.50
275	0.55
300	0.60
325	0.65
350	0.70
375	0.75
400	0.80
425	0.85
450	0.90
475	0.95
500	1.00

The equation for converting Units of Insulin to Volume (mL)

When using a Tuberculin Syringe draw up U500 insulin in ***volume (mL)***

units insulin ÷ 500 = volume of insulin measured on syringe in mL

Example: 250 units ÷ 500 = 0.5 mL

medication and is not used in the emergency department.

In an attempt to ensure that each step of the process is completed, the pharmacist checklist was modified to include notification of the CDEs. A nursing checklist is being developed to define responsibilities of and facilitate the procedure for nursing.

The order set is also being revised. The verification will be separated from the physician's order. Both the verification and physician's order will include sections for the standard mealtime dosing of U-500 and "corrective" U-500 insulin dosing. The back of the physician's order set will include prescribing information based on published recommendations[1,2] and a section on unit-to-volume conversion. The criterion calling for a physician to manage hypoglycemia will be for any blood glucose values of less than 70 mg/dL, and 2 a.m. point-of-care blood glucose concentrations will be monitored for the first 48 hours of treatment to assess for nocturnal hypoglycemia.

Further, the policy and procedure for adult patients will be shared with the pediatric hospital for consideration and presentation to the pediatric pharmacy and therapeutics committee.

Conclusion

Safety precautions for hospital use of U-500 insulin employed a multilayered, multidisciplinary process using safeguards at every step in the medication management process.

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Appendix—Pharmacist checklist for U-500 insulin

- ___ Dose is verified with the patient and documented on the order form
- ___ Order is written on the U-500 insulin order form, and dose is specified in both units and milliliters
- ___ Two-pharmacist order-entry process is followed
- ___ Patient label affixed to the vial is highlighted to differentiate it from other medications, and warning labels are affixed
- ___ Drug is hand delivered by pharmacist to charge nurse and bedside nurse **together**
- ___ Safety time-out
  - ___ Pharmacist and nurses review the U-500 insulin order and medication administration record
  - ___ Pharmacist provides education about key characteristics of U-500 insulin and supplemental information
  - ___ Pharmacist emphasizes proper administration and policy and procedure highlights
  - ___ U-500 insulin is placed in the individual patient's secure medication storage area
  - ___ Warning labels are placed on the charts and the secure medication storage area