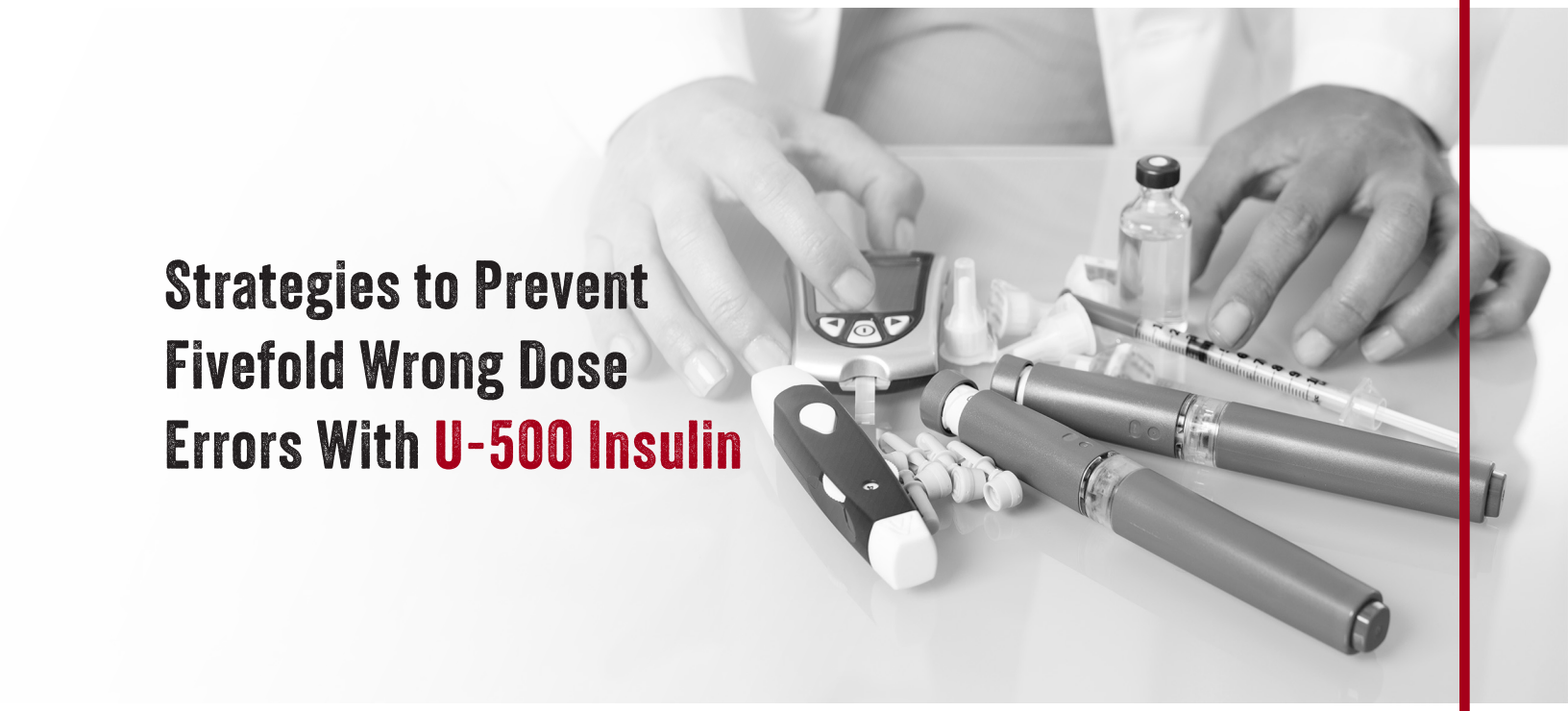
Strategies to Prevent Fivefold Wrong Dose Errors With U-500 Insulin



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Over the years, the Patient Safety Authority (PSA) has highlighted numerous errors involving insulin.[1-5] Recently, PSA has received several reports via the Pennsylvania Patient Safety Reporting System (PA-PSRS) describing errors with U-500 insulin that led to patients receiving either five times less or five times more insulin than intended. Humulin R U-500, a type of insulin that is five times more concentrated than U-100 insulin, is used to manage blood glucose levels in individuals with diabetes mellitus requiring more than 200 units of insulin per day.[6,7] As a high-alert medication,[8] U-500 insulin has been associated with dose errors that can lead to life-threatening hypoglycemia or hyperglycemia.[6]

There are many ways in which wrong dose errors can occur with insulin. The unique measurement system of insulin using "units" instead of the conventional milliliter (e.g., 1 mL=100 units) inherently complicates its dosing.[2,3,5] The potential for errors is further amplified by the availability of various formulations, concentrations, and delivery devices.[1,2,7,9-14] In the recent PA-PSRS reports, fivefold wrong dose errors with U-500 insulin occurred after the patients' home dose of insulin was incorrectly reconciled during admission to facilities that use 1 mL tuberculin or U-100 syringes to administer U-500 insulin. Presently, the U.S. Food and Drug Administration advises that U-500 insulin should only be administered using specifically designed U-500 syringes.[15]

Keywords: medication error, medication safety, patient safety, concentrated insulin, insulin overdose, insulin underdose, Humulin R U-500

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Example of Underdose Reported to PA-PSRS

Some patients use 1 mL tuberculin or regular U-100 syringes to measure their U-500 insulin at home. Because U-500 is five times more concentrated than U-100 insulin, the prescribed dose needs to be divided by five to be measured correctly with a U-100 syringe.[13] However, in some cases, when patients were admitted the markings on the syringe, which reflect the volume administered at home, were documented and ordered rather than the actual number of units prescribed. For example, a patient who takes 200 units/0.4 mL of U-500 insulin at home was ordered 40 units at the hospital. This resulted in a fivefold underdose.

Example of Overdose Reported to PA-PSRS

Other patients use U-500 pens or U-500 syringes at home, which do not require the dose conversion. When these patients were admitted, the patients' home dose in units was inadvertently documented as volume to be administered using the U-100 syringe. For example, a patient taking 75 units via U-500 pen at home was administered 0.75 mL (375 units) rather than 75 units (0.15 mL). This resulted in a fivefold overdose.

To prevent wrong dose errors with U-500 insulin, healthcare facilities should consider implementing the action items below.

- During medication reconciliation, confirm the type(s) of insulin, the concentration(s), the dose(s) in terms of units, and the delivery method used at home. Ask the patient to bring in the medication if possible and demonstrate their self-administration technique of insulin.[1,9,16]
- Reevaluate the facility's formulary[2] and evaluate the feasibility of using pens to administer U-500 insulin.[9,11]
- If the facility uses U-500 insulin vials instead of pens,
    - Use only U-500 syringes to measure U-500 insulin.[6,15]
    - Store U-500 vials at the pharmacy in a location separate from other insulins.[1,2,10,12,17]
    - Require both the units AND the volume (milliliters) in the medication order.[2,10,12]
    - Provide a prescription for U-500 syringes upon discharge to patients who were previously using a U-100 or tuberculin syringe.[13]
- Implement a prominent alert within the computerized provider order entry system to notify healthcare providers of the high-alert classification[1,8] of U-500 insulin (e.g., "Concentrated regular insulin U-500 provides 500 units per mL, which is 5 times the concentration of regular insulin U-100.")
- Require barcoded medication administration and documentation of an independent double check prior to administration.[1,2,10]
- Dispense patient-specific doses from the pharmacy with a barcoded label.[2,10-12,17]
- Consult an endocrinologist or other specialist trained in glycemic management for prescribing and adjusting therapy with U-500 insulin as determined by the organization.[10,17]
- Incorporate other members of the interdisciplinary team, such as certified diabetes educators, to provide comprehensive patient education on U-500 insulin safety and injection technique.[10,12,17]
- Provide ongoing education to both providers and patients regarding insulin products and related safety events.[1,2,9,12,17] Maintain up-to-date and comprehensive drug information resources relating to insulin within the facility.

References

1. Patient Safety Authority. Complexity of Insulin Therapy. *Pa Patient Saf Advis*. 2005;2(2):30-1.

2. Patient Safety Authority. Medication Errors With the Dosing of Insulin: Problems Across the Continuum. *Pa Patient Saf Advis*. 2010;7(1).

3. Patient Safety Authority. Overdoses Caused by Confusion Between Insulin and Tuberculin Syringes. *Pa Patient Saf Advis*. 2004;28:1-2.

4. Patient Safety Authority. The Current State of "Wrong Patient" Insulin Pen Injections. *Pa Patient Saf Advis*. 2015;12(3):110-15.

5. Patient Safety Authority. Treating Hyperkalemia: Avoid Additional Harm When Using Insulin and Dextrose. *Pa Patient Saf Advis*. 2017;14(3).

6. National Library of Medicine. Label: HUMULIN R U-500 - Insulin Human Injection, Solution. Dailymed. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b60e8dd0-1d48-4dc9-87fd-e14675255e8c. Updated February 22, 2024. Accessed April 1, 2025.

7. American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2025. *Diabetes Care*. 2024;48(Supplement_1):S181-S206. doi: 10.2337/dc25-S009.

8. Institute for Safe Medication Practices. ISMP List of High-Alert Medications in Acute Care Settings. 2024. Available from https://www.ismp.org/sites/default/files/attachments/2024-01/20240111.pdf.

9. Donihi AC, Moorman JM, Abla A, et al. Pharmacists' Role in Glycemic Management in the Inpatient Setting: An Opinion of the Endocrine and Metabolism Practice and Research Network of the American College of Clinical Pharmacy. *JACCP J Am Coll Clin Pharm*. 2019;2(2):167-76. doi: 10.1002/jac5.1041

10. Monroe PS, Heck WD, Lavsa SM. Changes to Medication-Use Processes After Overdose of U-500 Regular Insulin. *Am J Health-Syst Pharm*. 2012;69(23):2089-93. doi:10.2146/ajhp110628

11. McKay C, Schenkat D, Murphy K, Hess E. Review of Medication Error Sources Associated With Inpatient Subcutaneous Insulin: Recommendations for Safe and Cost-Effective Dispensing Practices. *Hosp Pharm*. 2022;57(6):689-96. Epub 2022/11/08; doi:10.1177/00185787221095771; PubMed PMID: 36340627; PubMed Central PMCID: PMCPMC9631006

12. Samaan KH, Dahlke M, Stover J. Addressing Safety Concerns About U-500 Insulin in a Hospital Setting. *Am J Health-Syst Pharm*. 2011;68(1):63-8. doi:10.2146/ajhp100224

13. Sze D, Goldman J. Human Regular 500 Units/mL Insulin Therapy: A Review of Clinical Evidence and New Delivery Options. *Clin Diabetes*. 2018;36(4):319-24. Epub 2018/10/27; doi:10.2337/cd18-0004; PubMed PMID: 30364062; PubMed Central PMCID: PMCPMC6187959

14. Cohen MR. Pharmacists' Role in Ensuring Safe and Effective Hospital Use of Insulin. *Am J Health-Syst Pharm*. 2010;67(16_Supplement_8):S17-S21. doi:10.2146/ajhp100173

15. Food and Drug Administration. FDA Approves a Dedicated Syringe To Be Used With Humulin R U-500 Insulin. FDA. https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-dedicated-syringe-be-used-humulin-r-u-500-insulin. Published July 8, 2016. Accessed April 1, 2025.

16. ISMP Canada. Dose Confusion When Switching Between Insulin Delivery Devices. *ISMP Canada Safety Bulletin*. 2019;19(9).

17. Institute for Safe Medication Practices. ISMP Guidelines for Optimizing Safe Subcutaneous Insulin Use in Adults. ECRI. https://home.ecri.org/blogs/ismp-resources/guidelines-for-optimizing-safe-subcutaneous-insulin-use-in-adults. Published June 5, 2017. Accessed April 1, 2025.

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