

# Acute Care

# ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

## Adverse glycemic events and critical emergencies



**PROBLEM:** For years, insulin errors have been linked to harmful adverse events, often resulting in serious hypoglycemia or hyperglycemia. Glycemic management in patients with diabetes and/or the acutely ill who are receiving insulin can be challenging, especially since the frequency and timing of necessary blood glucose assessments are often patient specific. Furthermore, communication breakdowns; inaccurate home medication lists; untimely medication reconciliation; insulin mix-ups; and delays in assessments, nutritional intake, and initiation of glycemic management protocols, may lead to a critical medical emergency and can also complicate care during such emergencies.

To further investigate these situations, **ECRI and the Institute for Safe Medication Practices (ISMP) Patient Safety Organization (PSO)** analyzed 100 adverse glycemic events reported to the PSO between May 2018 and April 2020 that led to or occurred during a critical medical emergency, such as a rapid response team call or a cardio-pulmonary arrest. All of the analyzed events fell within category E (temporary harm) through I (death) according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index for Categorizing Medication Errors ([www.ismp.org/ext/816](http://www.ismp.org/ext/816)). The key contributing factors, along with a few examples of the reported errors, are summarized below.

### Key Contributing Factors

**Omissions or delays in initiating glycemic management protocols.** In approximately 30% of the analyzed events, hypoglycemia and hyperglycemia management protocols did not exist, were not ordered, or were not initiated when indicated, leading to a failure in addressing blood glucose values below or above normal limits. In some cases, prescribers were unaware of low or high blood glucose levels, and a glycemic management protocol and/or treatment was not initiated until the patient's condition deteriorated.

*The blood glucose level of an unresponsive hospitalized patient with a history of hypoglycemia was checked using a glucose meter and was found to be 55 mg/dL. The patient failed to respond to repeated attempts to arouse her, including a sternal rub, so a rapid response team was called. Still unresponsive, the patient was transferred to a critical care unit. However, a glycemic management protocol was never initiated, and treatment with a rescue agent (intravenous [IV] dextrose) was not provided. Additionally, no further measurement of the patient's blood glucose was ordered or obtained.*

**Medication administration issues.** Administration issues caused by look-alike insulin names or label mix-ups and/or knowledge deficits accounted for approximately 25% of the analyzed glycemic events. A few errors were associated with documentation issues or too-rapid administration of an IV 50% dextrose solution leading to infiltration and phlebitis. However, most administration-related errors involved giving the wrong type of insulin (long-acting vs. short-acting), the wrong dose of insulin, or the wrong drug (i.e., administering insulin instead of the prescribed medication).

**Insulin administered without consideration of dietary intake.** Nearly 20% of the analyzed events were associated with patients receiving their usual full dose of insulin despite being NPO or unable to consume a meal in a timely manner after receiving

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## SAFETY briefs



**Errors with injectable specialty medications.** ISMP has received numerous reports of errors and hazards related to the quantity and package size of specialty medications. To cite one example, an outpatient pharmacy dispensed two syringes of **STELARA** (ustekinumab) 45 mg/0.5 mL because the data entry technician mistakenly entered a quantity of "1" for one syringe, not realizing that Stelara is billed (and dispensed) per mL. This resulted in 1 mL, or two syringes, being dispensed.

According to the National Council for Prescription Drug Programs (NCPDP) Billing Unit Exception Task Group, liquid medications (including injectables) are dispensed based on standardized "billing units." The "milliliter" (mL) billing unit is used when a product is measured by its liquid volume, as seen with Stelara (**Figure 1**). However, injectable products may also be billed as



**Figure 1.** Stelara carton contains one syringe (0.5 mL), with a "milliliter" billing unit of 0.5 mL.

a "kit" containing a single syringe or pen with an alcohol swab, or a tray containing multiple syringes or pens with alcohol swabs ([www.ismp.org/ext/817](http://www.ismp.org/ext/817)). One challenge with selecting the correct billing unit is that pharmacy staff may not be aware of the exact contents inside the carton since these are usually not opened.

To learn more about specialty medication quantity and package size errors and hazards, ISMP sent a targeted 5-question survey to 36 specialty pharmacies. Sixty-four percent (N=23) of pharmacies responded to the survey. Ninety-six percent

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insulin. More than half of these patients were prescribed prandial (meal-related) and basal (long-acting) insulin, but the doses were not adjusted to account for their dietary intake.

*A rapid response team was called to the bedside of an unresponsive patient who was seizing. The patient's point-of-care blood glucose was only 23 mg/dL at that time. A nurse began administering a 50% dextrose solution IV, and within 3 minutes, the patient was alert and her blood glucose was 100 mg/dL. The patient had received her prandial insulin (11:00 a.m.) more than 2.5 hours before lunch arrived on the unit. The patient was then encouraged to eat a full lunch.*

**Omissions or delays in monitoring patients.** In nearly 15% of the analyzed events, healthcare practitioners failed to order blood glucose monitoring when it was indicated, failed to perform (or document) blood glucose monitoring despite specific orders, or were never notified regarding critical blood glucose values.

*A rapid response team was called for a patient with diabetes with hypoxic respiratory failure. The patient was treated with oxygen supplementation and 10% dextrose solution IV and then transferred to an intensive care unit, where no point-of-care glucose monitoring was ordered or performed. The next day, the patient's laboratory blood glucose value was 62 mg/dL in the morning and 33 mg/dL in the afternoon; however, the attending physician was never notified by the laboratory or the primary care nurse of the critically low glucose value of 33 mg/dL, and the patient was never treated. Several days later, when the patient experienced a cardiopulmonary arrest, a venous blood glucose was drawn which was 30 mg/dL. The patient became totally unresponsive and was placed on life support.*

**Home medication history and reconciliation errors.** Six percent of the events were related to errors associated with obtaining an accurate list of home medications used for glycemic management upon hospital admission, or untimely medication reconciliation. In one event, medication reconciliation and prescribing of a new patient's antidiabetic medications taken at home did not occur until 24 hours after admission. These events resulted in suboptimal glucose management during hospitalization or upon discharge.

*A patient taking insulin at home was hospitalized for an unrelated condition. During hospitalization, he was switched to oral antidiabetic medications with positive glycemic outcomes. The attending physician prescribed these oral medications upon discharge, intending for the patient to discontinue the insulin. Because medication reconciliation did not occur at discharge, the patient did not know to stop taking insulin. The patient continued taking insulin at home, as well as his newly prescribed oral antidiabetic medications, resulting in significant hypoglycemia and hospital readmission.*

**Other contributing factors.** A few (4%) of the analyzed events were related to other contributing factors. These included glycemic management processes that had not been clearly established, such as failing to address the possibility of hypoglycemia in patients receiving IV insulin for a PET (positron emission tomography) scan viability study. Another contributing factor included rescue medications that were unavailable due to shortages.

**SAFE PRACTICE RECOMMENDATIONS:** Based on the contributing factors uncovered during our analysis of adverse glycemic events, implement the following best practices:

**General/Operational**

**Develop glycemic management protocols.** Establish standard protocols and/or order sets to guide the treatment and monitoring of clinically significant hypoglycemia and hyperglycemia, including hyperosmolar hyperglycemic state and diabetic ketoacidosis.

**Ensure rescue agents are available.** Ensure appropriate rescue agents (e.g., juice, glucose gel, glucagon, 10% or 50% dextrose) are readily available to clinicians, with

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of the respondents indicated that they were aware of errors or close calls related to specialty injectable medication quantities or package sizes. The most common concerns were associated with confusion regarding whether the billing standard was based on "milliliters" or "kits," actual starter pack quantities, and when multiple syringes were needed for one dose. The specialty medications cited most frequently by respondents as being involved in events were **DUPIXENT** (dupilumab), **HUMIRA** (adalimumab), **CIMZIA** (certolizumab pegol), and **SKYRIZI** (risankizumab-rzaa).

The specialty pharmacy respondents provided valuable insights into strategies they have implemented to prevent quantity and package size-related errors. One in three pharmacies indicated that they use dispensing software notes to alert the team to the correct package size for specific products (e.g., quantity 1 = 2 syringes). Nearly one in five pharmacies requires two pharmacists to double check/verify the entry of all orders for specialty drugs. Two pharmacies suggested the use of a proactive risk assessment to evaluate the package size prior to dispensing a new medication, and two pharmacies also reported that they employed barcode scanning to catch package size discrepancies. Other notable strategies include clarifying the billing unit as "mL" vs. "kit" in the dispensing system, adding a default package size to the dispensing software, configuring the computer system to print the number of labels based on the number of packages needed, and taping packages together.

If you dispense specialty medications, consider implementing some of the above strategies. If you prescribe specialty medications, or other injectable medications, be sure to include the units (mL vs. syringe vs. box vs. kit) with the quantity to minimize pharmacy staff confusion.

**Surprise! Not all drug labels have an NDC.**

**HECTOROL** (doxercalciferol) injection is a synthetic vitamin D analog indicated for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on dialysis. The product is available in single-dose vials in cartons of 50, either as 2 mcg per mL or 4 mcg per 2 mL.

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directions for when to use each rescue agent, proper administration to treat adverse glycemic events, and follow-up. During shortages, suitable alternatives should be available.

**Take steps to avoid insulin mix-ups.** Limit the number of different types of insulin on the formulary, and avoid close storage of medications with look-alike names or labeling/packaging. Display both the generic and brand names of insulin products on computer screens, labels, and any other format used to communicate the drug names in the facility. Also, use tall man lettering with bolded text for the unique letter characters of look-alike insulin names (e.g., Huma**LOG** and Humu**LIN**; Novo**LOG** and Novo**LIN**) when displayed in computer order entry systems, order sets, protocols, guidelines, medication administration records, automated dispensing cabinet (ADC) screens, infusion pump screens, drug storage bins, and hospital pharmacy labels.

**Dispense hyperkalemia kits.** Have the pharmacy dispense a hyperkalemia kit to patient care units, which includes a 3 mL vial of regular insulin (or a standard rapid-acting insulin); alcohol swabs; 50% dextrose injection; an insulin syringe that allows needleless IV administration; directions for preparation, administration, and patient monitoring requirements; and a label for the syringe (to apply after preparation but before administration).

**Upon Patient Admission**

**Obtain the best possible medication history.** Carry out a good faith effort to capture a thorough and comprehensive medication history upon admission. Verify the medications, doses, indications, and adherence to medications on the patient's home medication list using multiple resources (e.g., outpatient pharmacy records, prior admission documentation, discharge history, interview of family members, review of actual medication containers). Always actively involve the patient and/or caregiver, if possible.

**Ensure timely medication reconciliation.** Require a verified home medication list, medication reconciliation, and the prescribing of necessary home medications as soon as possible after hospital admission.

**Hypoglycemia and hyperglycemia risk assessment.** Require the admitting nurse to conduct a risk assessment of all patients receiving insulin upon admission and periodically thereafter to identify individuals at high risk for developing hypoglycemia (e.g., low body weight, basal insulin dose greater than 0.25 units/kg, basal insulin-only dosing, concomitant oral antidiabetic medications, history of hypoglycemia) or hyperglycemia (e.g., infection, pancreatitis, trauma, alcohol abuse), and specifically target these patients for preventative interventions.

**Prescribe needed blood glucose monitoring.** For patients with diabetes mellitus or requiring critical care or procedures, assess the patient's need for point-of-care or venous blood glucose monitoring and assessments, and order these as needed. Ensure the electronic health record (EHR) compiles any orders for glucose monitoring and assessments in one designated place so it is accessible to all clinicians. Discuss blood glucose monitoring results during patient care rounds and during staff communications.

**Initiate protocols.** Initiate glycemic management protocols/order sets for all patients with diabetes mellitus, non-diabetes critical care patients receiving insulin, and/or any patient who experiences a point-of-care or venous blood glucose value above or below a specific target value.

**During Hospitalization**

**Coordinate meal delivery.** In conjunction with meal delivery, develop a coordinated process to promote timely blood glucose checks (no longer than 1 hour before meal delivery, 0 to 30 minutes is preferred) and administration of prandial insulin (within 15 minutes of the start of a meal).

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There is also a 4 mcg per 2 mL multiple-dose vial, also in a carton of 50. While the package insert lists a National Drug Code (NDC) number for the vial labels, the NDC number is not printed on the container label itself (**Figure 1**). There is an NDC number on the outer carton, but bedside



**Figure 1.** The vial labels for Hectorol (Sanofi Genzyme) do not list an NDC number.

or dialysis staff typically do not have access to the carton label. The vials have linear and 2D barcodes, but the barcodes may not always scan properly. Also, a human readable NDC number is often used when a recall is issued. You would need the NDC number and the lot number to identify and quarantine recalled products, which can be checked manually.

Sanofi Genzyme, the manufacturer of Hectorol, noted that the US Food and Drug Administration (FDA) regulations do not require an NDC number to be on all labeling. Surprisingly, that is correct. While the FDA requests that the NDC be present on product containers (§201.2 Drugs and devices; National Drug Code numbers, [www.ismp.org/ext/797](http://www.ismp.org/ext/797)), this is not required on all labels and/or drug labeling. Even so, we agree with the reporter that all information, including the NDC, should be visually readable to provide the appropriate information readily and easily to healthcare professionals providing care to patients. We have asked FDA to request that the company add the NDC to the immediate container label and include the NDC in the linear and 2D barcode in a manner that is human readable. We also asked FDA to work toward revising the regulation to require the NDC on all packaging and vial container labels.

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**Assess nutrient intake before insulin administration.** Before insulin administration, require practitioners to assess the patient's nutrient intake, including the time and the amount eaten at the last meal, and the timing of the next meal. Consider using a system of alerting the dietary staff (e.g., colored menus) to monitor meal consumption and/or to notify a nurse when delivering a tray to a patient receiving prandial insulin.

**Assess nutrient intake for changes in eating.** Establish a standardized process to alert an authorized prescriber regarding any significant changes in a patient's carbohydrate intake, which may require an adjustment of the usual insulin doses. Insulin doses, including prandial and basal doses, should only be held or modified with a prescriber's order or via explicit directions in an existing protocol or order set.

**Employ barcode scanning.** Utilize bedside barcode scanning technology prior to drug administration to verify the drug and patient.

**Centralize information.** Ensure all patient-specific, diabetes care-related information, including blood glucose values and significant changes in carbohydrate intake (e.g., NPO status, changes in enteral or parenteral nutrition), is located in one designated place within the patient's EHR so it is accessible to all clinicians. This may involve collaboration with your respective EHR vendor and informatics staff.

**Communicate critical blood glucose values.** Define clinically significant hypoglycemia parameters in terms of symptoms and blood glucose levels at which prescribers should be notified. Also, establish critical blood glucose values at which the laboratory staff are required to notify a specified practitioner (e.g., primary care nurse, prescriber).

### Managing Glycemic Events

**Permit emergency treatment.** Establish protocols and/or coupled order sets that permit the emergency administration of an appropriate rescue agent by a qualified clinician for clinically significant hypoglycemia based on identified symptoms and/or a specified minimum blood glucose level. Investigate and track the use of rescue agents as a potential opportunity to improve overall glycemic control.

**Treatment of clinical symptoms.** Provide care to patients based not only on their venous or point-of-care blood glucose values, but also according to their clinical symptoms and preexisting conditions, even when their symptoms are inconsistent with a current blood glucose value.

**Reassessment.** Establish a minimum and maximum blood glucose value (point-of-care or venous) that prompts a prescriber to conduct a patient, nutrition, and drug therapy reassessment to determine if modification of the diet and/or glycemic management treatment is warranted. If a pattern above or below the established blood glucose values occurs, consider requiring a team of prescribers, nurses, pharmacists, and dietitians to conduct the reassessment in a collective manner.

**Consultation.** For patients with uncontrolled hyperglycemia or hypoglycemia, consider consulting an endocrinologist or clinician trained in diabetes or insulin management.

### Upon Discharge

**Educate the patient.** Upon discharge, educate patients/caregivers about any changes in their pre-hospitalization home medication list, highlighting discontinued or newly prescribed medications.

### Other

**Additional recommendations.** The *ISMP Guidelines for Optimizing Safe Subcutaneous Insulin Use in Adults* ([www.ismp.org/node/93](http://www.ismp.org/node/93)) can be accessed for additional recommendations to help prevent insulin errors and improve patient outcomes.

## Special Announcements

### December 10 assessment deadline

Surgery sites have 1 more week to submit their findings from the *ISMP Medication Safety Self Assessment<sup>®</sup> for Perioperative Settings* to ISMP. For details, visit: [www.ismp.org/node/18027](http://www.ismp.org/node/18027). If you have questions about the data submission process or need more time to participate, please contact: [selfassess@ismp.org](mailto:selfassess@ismp.org).

### FREE ISMP webinars

ISMP is presenting two **FREE** webinars on high-alert medications! The first webinar covering **insulin and vasopressors** will be presented on **December 16, 2021**, and the second webinar covering **heparin, concentrated electrolytes, and magnesium** will be presented on **January 25, 2022**. Continuing education (CE) credit will be provided. For the December webinar, visit: [www.ismp.org/node/28249](http://www.ismp.org/node/28249), and for the January webinar, visit: [www.ismp.org/node/28440](http://www.ismp.org/node/28440).

### FREE FDA webinar series

The US Food and Drug Administration's (FDA) Division of Drug Information is presenting a **FREE** webinar, *FDA Drug Topics: Overview of Expanded Access (EA) Program and EA eRequest Site*, on **December 14, 2021**. For details, visit: [www.ismp.org/ext/30](http://www.ismp.org/ext/30), and to register, visit: [www.ismp.org/ext/31](http://www.ismp.org/ext/31).

### Register for our virtual CHEERS AWARDS!

Please join ISMP on **December 7, 2021**, at 6:00 p.m. ET, for our **virtual CHEERS AWARDS** celebration. To register for the free event, visit: [www.ismp.org/node/25790](http://www.ismp.org/node/25790).

To subscribe: [www.ismp.org/node/10](http://www.ismp.org/node/10)



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Call 1-800-FAILSAF(E) or visit our website at: [www.ismp.org/report-medication-error](http://www.ismp.org/report-medication-error). ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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