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Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Enhancing Antithrombotic Stewardship by Optimizing Clinical Decision Support—Part II

Problem: In **Part I** of our newsletter, Antithrombotic Therapy—Advancing Stewardship Beyond Anticoagulation, we highlighted the need to shift from traditional anticoagulant monitoring to a comprehensive antithrombotic stewardship program. We also shared recent events reported to ISMP and recommended safe practices to consider when implementing or expanding your antithrombotic stewardship program. In **Part II,** we focus on how one organization, Brown University Health, identified gaps in its program, customized its electronic health record (EHR), and built clinical decision support (CDS) to maximize the use of its resources.

Identifying Gaps in Antithrombotic Oversight

Brown University Health is comprised of three acute care hospitals in Rhode Island and two in Massachusetts with over 1,400 licensed beds. In 2022, Brown University Health began to expand services beyond traditional inpatient anticoagulation monitoring done by unit-based pharmacists. Those efforts resulted in a pharmacy antithrombotic stewardship program, which started with one dedicated full-time pharmacist position providing clinical services Monday through Friday. The development phase of the antithrombotic stewardship program included assessing current practices and optimizing the EHR.

Initially, the pharmacist identified that there was no consistent, integrated method to easily identify patients receiving antithrombotic medications, leading to inconsistencies in pharmacist interventions and oversight. Key safety concerns reported included the following:

- Out-of-range international normalized ratio (INR) events
- Inappropriate direct thrombin inhibitor therapy
- Overuse of blood factor products
- Underdosing of direct oral anticoagulants (DOACs)
- Enoxaparin prescribed without dose adjustment for renal dysfunction
- Heparin infusions outside of therapeutic goal
- Unnecessary triple therapy with anticoagulation and dual antiplatelet therapy

A primary initial focus was to develop an infrastructure within the EHR for the antithrombotic stewardship pharmacist to readily identify patients receiving antithrombotic medications that met identified high-risk criteria for review and clinical intervention. With optimization of the EHR for patient identification and streamlined workflow, in 2023, the antithrombotic stewardship program was expanded to reach more patients throughout the system. In 2024, approval was granted for a second full-time pharmacist position, enabling the program to optimize patient outreach and extend services beyond weekdays to incorporate limited weekend coverage.

Despite significant growth during the early years of the program, the lack of true 24/7 coverage within the acute care space was identified as a gap. The team saw this need as an opportunity to develop CDS tools that would help practitioners identify and address major safety concerns with both anticoagulant and antiplatelet therapy for a comprehensive approach to antithrombotic stewardship. The optimization of CDS tools required an upfront lift to implement, but has a lasting effect without the need for daily oversight by a dedicated pharmacist. This approach to antithrombotic stewardship can be adopted by health systems regardless of the presence of dedicated pharmacist positions.

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SAFETY briefs

Five-Fold U-500 Insulin Overdose—Do Not Draw Up Dose from a Pen Cartridge. A patient received 250 units of U-500 insulin instead of 50 units as prescribed. A nurse drew up the dose from a **HUMULIN R U-500 KWIKPEN** (500 units/mL regular insulin [3 mL] pen) using a U-100 insulin syringe rather than administering it directly from the U-500 KwikPen using a disposable pen needle. A pharmacist monitoring the patient identified that they were experiencing hypoglycemia and contacted the nurse to inquire how the insulin had been administered, at which point the error was identified. The prescriber was notified, the patient was given oral glucose and intravenous (IV) dextrose, and their hypoglycemia resolved.

After Lilly discontinued the **HUMULIN R U-500** (500 units/mL regular insulin [20 mL]) multidose vials, the reporting organization converted to the KwikPen. This was the first patient requiring U-500 insulin after the transition. Previously, pharmacy supplied U-500 insulin doses in patient-specific syringes. Prior to switching to the KwikPen, the organization performed a multidisciplinary failure mode and effects analysis (FMEA) to identify risks associated with this transition. As a result, they added a warning icon to the medication administration record (MAR) that included extensive administration instructions and linked a tip sheet directly to the KwikPen orders. Education had been distributed via a nursing newsletter, but completion was not mandatory for nurses. In addition, the nurse who prepared and administered the dose was a travel nurse who had not received the education. Due to a system glitch, the KwikPen order did not prompt the pharmacy to dispense pen needles, and the nurse did not contact pharmacy to inquire about them.

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Safe Practice Recommendations: We encourage organizations seeking to expand their antithrombotic stewardship programs to learn from Brown University Health's experience and consider the following recommendations.

Project oversight. Brown University Health gathered an interdisciplinary team to evaluate current processes and opportunities for improvement. The team was led by an antithrombotic stewardship pharmacist and included collaboration from other pharmacists, medication safety, hospital leadership, hematology, laboratory medicine, and information technology (IT). The program was supported by their antithrombotic pharmacy and therapeutics (P&T) subcommittee, which reports to their P&T committee. The team reviewed published literature and guidelines and incorporated these recommendations into their organizational policies and procedures.[1,2]

Maximize use of resources. Brown University Health strategically allocated resources to improve CDS alerts within the EHR, refine best practice advisories, and implement indication-based prescribing of antithrombotic agents. This required an initial investment of resources to build the automation, but it streamlined EHR workflows and reduced practitioners' reliance on manual data review, thereby enhancing clinical practice efficiency.

Leverage the EHR. The team aimed to optimize the EHR upfront to help practitioners identify high-risk patients who were prescribed antithrombotic therapy and notify users of potential concerns so they could enhance care. They discovered that pharmacists often recognized certain risks during chart reviews, which served as early warning signs. The common findings were then incorporated into automated CDS. Instead of relying on manual checks, the EHR now proactively alerts practitioners to potential safety issues, such as:

- When a patient's laboratory result indicates a high risk of bleeding (e.g., INR greater than 4)
- When a newly prescribed drug may cause a harmful interaction with their antithrombotic therapy
- When a patient is incorrectly prescribed duplicate anticoagulant therapies
- Removal of pharmacologic venous thromboembolism (VTE) prophylaxis options from the admission order set when a patient is on warfarin prior to admission and has a recent INR greater than 2

The alerting strategies were built into the EHR function and customized based on the workflow of end users (e.g., nurses, prescribers, pharmacists) and the hospital's formulary. This automation helped ensure critical safety issues were addressed promptly, enhancing patient care and improving efficiency.

Optimize reversal agents. After identifying the high use of reversal agents like **KCENTRA** (prothrombin complex concentrate [(Factors II, VII, IX, X), Protein C, and Protein S]), the team completed a medication-use evaluation and based on this information, updated their guidelines to streamline the restriction criteria for use. They also updated the applicable order sets with additional CDS, including required fields (e.g., indication, anticoagulant being reversed, type of bleed, type of procedure).

Educate practitioners. Brown University Health provides antithrombotic education during onboarding for the inpatient pharmacist team, including how to manage the warfarin protocol, antithrombotic-related patient monitoring, antithrombotic-related guidelines, and an overview of the EHR antithrombotic order sets. Prescribers and nurses receive education through written information and presentations during formulary changes and protocol updates.

Enhance transitions of care. Antithrombotic pharmacists collaborate with transitions of care pharmacists to standardize practices and assist with hospital discharge. Brown University Health has outpatient warfarin clinics within the system that are also consulted during transitions of care. The transition of care pharmacist coordinates education for patients newly starting warfarin during inpatient admission, with plans to expand this to new start DOACs in the near future.

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This event highlights the need for manufacturers to notify customers and patients about planned changes in product availability to support safety and prevent errors. We warned of this risk when switching from vials to pens in our December 18, 2025 article, U-500 Regular Insulin Vial Discontinued. This error demonstrates that, even with proactive planning, latent system issues may still align perfectly with active failures of individuals and reach the patient. Organizations should learn from this event, and if you have not done so already, consider completing an FMEA to identify and mitigate risks. Review impacted systems (e.g., order sets, MAR, products in the pharmacy system, discharge prescriptions), related policies and procedures, and patient teaching materials to determine whether modifications are needed. Ensure that U-500 pen needles are readily available when U-500 insulin pens are used. Establish a communication and education plan and ensure that practitioners understand why drawing up a patient's dose from an insulin pen cartridge is unsafe. Gather feedback from staff and encourage them to report concerns and errors both internally and to ISMP for shared learning.

Difficult to Open HYDROmorphone Syringe Packaging. A practitioner reported concerns about **DILAUDID** (**HYDRO**morphone) 1 mg/mL prefilled syringes, manufactured by Fresenius Kabi (NDC 76045-009-01). The syringes have a "twist cap to open" design that serves as a tamper-evident seal, but the plastic overwrap does not reliably perforate or separate as intended, often requiring nurses at the reporting organization to cut the plastic to open (**Figure 1,** page 3). Additionally, when the practitioner twists the cap, the syringe plunger may become misaligned and loosen, sometimes resulting in the plunger falling out and the contents of the syringe spilling. The reporting organization noted that the ongoing opioid shortage has forced them to purchase alternative products, such as this particular syringe, increasing exposure to potential safety risks associated with the packaging design.

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Quality improvement. As a result of this antithrombotic project, the team achieved measurable progress toward established safety objectives. Weekly retrospective chart reviews revealed a 10% reduction in noncompliance with Kcentra formulary restriction over a two-year period. Furthermore, the team is systematically monitoring the following metrics:

- Increased pharmacist interventions for patients on antithrombotic medications (due to increased ability to identify high-risk patients)
- Increased accepted pharmacist interventions for patients on antithrombotic medications
- Decreased frequency of inpatient INRs greater than 5 for patients on warfarin therapy

Next steps. Brown University Health plans to expand blood factor stewardship, enhance transitions of care efforts, and optimize outpatient antithrombotic management reach.

Call to action. ISMP recommends that EHR vendors ensure their systems have a clear method for practitioners to identify at-risk patients and maximize antithrombotic CDS support. Without these standard safeguards, organizations are forced to create custom workflows that require extensive resources, while standard automated CDS could benefit all users.

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- **ISMP Safe Medication Management Fellowship**: This opportunity is for a healthcare practitioner (e.g., pharmacist, nurse, or physician) to work remotely with ISMP.

For more information, click here.

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Figure 1. Dilaudid syringe "twist cap to open" design by Fresenius Kabi is difficult to open, requiring nurses to cut the plastic overwrap.

We reached out to the manufacturer and the US Food and Drug Administration (FDA) to notify them about these packaging concerns and suggest that the product design be revised to ensure opening the cap functions as intended and does not accidentally displace the plunger, resulting in medication spillage. Notify staff of this risk and educate them to follow the prescribing information, which recommends that users hold the syringe outer packaging with both hands. To break the tamper-evident seal, hold the tube and the cap close to the seal, and twist until broken. Remove the cap of the outer packaging by pulling it straight away from the tube to avoid dislodging the plunger rod of the syringe. Report concerns and errors to the manufacturer and to ISMP.

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