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

Changing the Clock — Safety Challenges With Medication Order Retiming

Problem: Adjusting medication times due to clinical circumstances is a common requirement during the course of patient care. During order entry or verification, practitioners may need to modify standard order default times in the electronic health record (EHR) for a variety of reasons, including the patient's home medication schedule. In addition, practitioners may need to reschedule a single dose of medication without affecting the scheduled times for future doses, or they may need to reschedule two consecutive doses closer together to get the patient back on their dosing schedule. Alternatively, a practitioner may modify the ongoing, routine schedule of a medication (e.g., changing a 0900 dose to 0700) for all future doses if a situation arises warranting this decision (e.g., drug-drug interaction that requires medications to be given hours apart). A prescriber may also need to increase or decrease a patient's dose shortly after it has been administered. Depending on how the system is configured, the modified order may default to start immediately, even if that is not the intended schedule, thus requiring the order to be retimed.

Unclear organizational expectations regarding practitioner types (e.g., prescriber, pharmacist, nurse, respiratory therapist) permitted to adjust medication times and conditions for retiming doses can cause inconsistencies and errors (e.g., dose stacking leading to toxicity, omission/delay of critical medication). For example, if a particular pharmacist often takes responsibility for adjusting medication dose times upon order verification (as needed), a nurse may become accustomed to this and rely on all pharmacists to have a similar process, which may not be part of the standard pharmacist workflow. Depending on the practitioner, there could also be variability in how many doses are adjusted (e.g., one or two doses versus retiming an entire dosing schedule).

A prescriber may order a one-time dose and scheduled doses of a medication at the same time. Depending on how the EHR is configured, the order for the scheduled doses may not default to the appropriate start time, requiring a practitioner to adjust the time. Or, a prescriber may order a one-time dose of medication for a patient in the ED, and another prescriber may order scheduled doses of the same medication once the patient is admitted. Depending on the EHR functionality and configuration, the system may or may not alert practitioners or it may not be easily visible that the patient has already been administered a one-time dose and prompt for the new order to be retimed appropriately.

Practitioners may need to reschedule medications to a more appropriate time due to side effects (e.g., insomnia, drowsiness), patient discomfort (e.g., burning sensation, flushing), drug-drug or drug-food interactions, a laboratory result, or an inability to administer the medication on time due to a scheduled conflict. Rescheduling may be needed if a prescriber orders a medication with instructions to be given at a particular time related to a procedure or other treatment (e.g., a contrast agent to be administered one hour prior to an imaging study that was rescheduled, or a premedication timed 30 minutes prior to a chemotherapy infusion that is pending the patient's laboratory results). The following examples illustrate retiming events reported to ISMP.

Errors Reported to ISMP

A prescriber ordered 1 g of oral acetaminophen as a one-time dose to be given now and also ordered 1 g every 6 hours as needed (PRN) for pain. The system did not default the second order to

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Diluent Administered Without Alteplase. A prescriber gave a verbal order to a nurse for **ACTIVASE** (alteplase) 50 mg intravenous (IV) push, to manage a patient's pulmonary embolism during a code in the ED. The alteplase product (made by Genentech), which was stored in an automated dispensing cabinet (ADC), comes in a carton containing a 100 mL vial of sterile water for injection and another vial with 100 mg of alteplase powder that needs to be reconstituted prior to administration. A second nurse removed a vial from the ADC, and handed what was thought to be alteplase to a third nurse, who drew up and administered 50 mL, not knowing that the vial removed from the ADC only contained sterile water.

Since this was the last dose in the ADC, a stock out report was generated in the pharmacy notifying a pharmacy technician that the drug needed to be replenished. When refilling the ADC, the error was identified by the technician who noticed the Activase carton contained a full alteplase drug vial (powder) and no vial of diluent (which had been removed during the code). The pharmacy technician immediately told the pharmacist, who notified the prescriber of the error. The alteplase dose was then administered to the patient about 15 minutes after the sterile water was given. The patient had coded several times before the actual alteplase was administered. Return of spontaneous circulation was achieved, but the family later decided to withdraw support, and unfortunately, the patient expired.

Once the Activase carton is opened, the instructions for use contain a red stop sign with a warning, "Read before preparing Activase" (**Figure 1**, page 2); however, the hospital reported that there is not a prominent warning on the carton label

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begin 6 hours after the first dose, so both orders had the same start time. The nurse administered the one-time dose to the patient. Neither the prescriber, pharmacist, nor nurse retimed the PRN order to begin 6 hours after the one-time dose. The nurse administered the first PRN dose less than 4 hours after the one-time dose from the previous order. It is unknown whether an alert was issued to the prescriber, pharmacist, or nurse at any stage to indicate that acetaminophen was being prescribed or administered too early (less than 6 hours since the previous dose).

A prescriber ordered intravenous (IV) vancomycin every 12 hours with administration times at 0700 and 1900. The first dose was delayed and the nurse administered it at 0800. Later in the day, the nurse who administered the first dose rescheduled the next dosing time to 2000 from 1900, and then scheduled future doses starting the following day to ensure they were timed appropriately at 0800 and 2000. However, when doing so, this canceled the 2000 edit and pushed the next dose administration to 0800 the following day. The patient missed the 2000 dose and went 24 hours without receiving vancomycin. This led to a delay in time reaching the therapeutic range. In this organization, nurse rescheduling of medication doses does not require pharmacist verification and there was not a policy that specified if vancomycin needed to be rescheduled if administered one hour late.

Safe Practice Recommendations: While there are a variety of circumstances when medications must be retimed, organizations should enhance workflow to avoid this whenever possible. Consider the following recommendations to limit the risk of errors.

Assess current status. Gather an interdisciplinary team to understand the scope and potential scenarios of medication dose times being changed within your organization. Review safety reports and data to understand retiming practices based on practitioner type and medication and investigate the rationale. Ask for feedback from practitioners about situations that often require retiming and what barriers they face when doing so, to develop effective mitigation strategies for overcoming these obstacles.

Develop a policy. Create or reevaluate the organizational policy for medication timing adjustments. Ensure the policy includes guidance for adjusting dose times during order entry, verification, and retiming scenarios outside of new orders. Include what necessitates a medication being rescheduled, and which practitioner type is allowed to and is responsible for retiming medication orders as needed. Based on data and practitioner feedback, determine how to manage each type of timing adjustment scenario and clearly address each issue in the policy.

Evaluate EHR functionality. Understand the various ways that medications can be retimed in your EHR system, and the EHR rules for who (practitioner type) can make those changes. In some EHR system configurations, organizations can define when the system will require a pharmacist to review a medication order that has been rescheduled by another practitioner (e.g., prescriber, nurse, respiratory therapist) to verify appropriateness. Also, evaluate where one-time orders are displayed in the EHR (e.g., medication administration record [MAR], medication list) to ensure this information is visible for all practitioners at the appropriate times.

Review and update order sets. Evaluate how order sets are built to minimize the need for practitioners to retime doses. For scenarios that often require multiple orders of the same medication (e.g., acetylcysteine for acetaminophen overdose), link the orders with appropriate sequential start times, when applicable. If a medication requires a loading dose to be administered over 30 minutes, followed by a continuous infusion, ensure the continuous infusion order is set up to begin 30 minutes after the loading dose. Also, review scheduled frequencies and default times. For example, does "BID" default to 0700 and 1900, coinciding with nursing shift change? Avoid situations where it would be difficult for nurses to administer doses on time, particularly in certain units where they have several patients receiving multiple scheduled medications.

Optimize clinical decision support. Evaluate the clinical decision support alerts (e.g., a dose has been rescheduled too soon or too late) configured in the system, and ensure the appropriate

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specifying that this alteplase product needs to be reconstituted (**Figure 2**). Not knowing that the carton contained one vial of 100 mg of alteplase powder and one vial of 100 mL of sterile water diluent, the nurse who removed the vial from the ADC thought that each vial in the carton was ready to use and contained alteplase. From the time the verbal order was given to the time the sterile water was administered, there were several handoffs between nurses. Barcode scanning was available in the ED but was not used.

Figure 1. The carton includes a 100 mg vial of alteplase powder (top), a 100 mL vial of sterile water (bottom), and the instructions for use, which contain a red stop sign with a warning, "Read before preparing Activase."

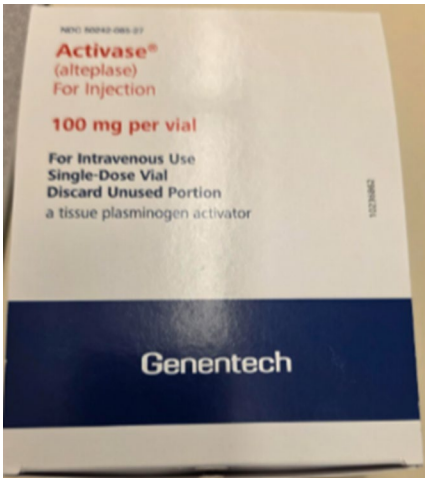

Figure 2. The Activase carton does not prominently state that the alteplase powder needs to be reconstituted with sterile water prior to administration.

We have reached out to the US Food and Drug Administration (FDA) and Genentech to notify them of this concern. If your

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practitioners are receiving applicable system warnings and addressing them at the appropriate time.

Reconcile medications. Evaluate the medication reconciliation process as it relates to the times that medications are scheduled during transitions of care (e.g., patients going to and from the operating room [OR], where medications are often held and need to be rescheduled for a later time). Reconcile all new postoperative medication orders with previously prescribed medications. Organizations and institutional leadership must have a formal process outlining the designated prescriber (e.g., hospitalist, surgeon) responsible for completing medication reconciliation during transitions of care (e.g., admission, transfer, procedure, discharge), including ordering the medications at the appropriate time.

Review medications daily. Encourage prescribers, pharmacists, and nurses to conduct a daily review of their patients' medication orders, including a review of potential schedule conflicts. Using the MAR for this review provides an additional opportunity to identify the frequency of PRN medications administered or the patient's (or family's) refusal of prescribed medications to ensure appropriate follow-up in the plan of care.

Educate practitioners. During orientation and annual competency assessments, educate staff about your organization's policy for medication timing adjustments and related EHR functionality. Provide practitioners with simulation-based education using scenarios to achieve specific learning objectives, including appropriate and inappropriate dose time adjustments based on common scenarios. Include examples of errors that have occurred and how to mitigate the risk. If the same EHR is not used throughout the health system, ensure practitioners understand how to view medication documentation if a drug is administered in a different care area (e.g., ED, OR). Encourage them to investigate any questionable medication times (e.g., delayed start, too close to the last dose) without an explanation on the MAR.

Educate patients. Inform patients, family members, and caregivers about their medication schedules and gather feedback to ensure the recommended timing is feasible for home use. Discharge documentation must be clear so that patients know what medications to take at a particular time and the rationale. Encourage them to reach out to their prescriber or pharmacist to discuss any changes to the times that they take their medications at home.

Learn from errors. Review internally reported medication retiming-related errors as well as published external events such as those described in this newsletter. Encourage all staff to report close calls and actual errors that have reached patients. Communicate actions that have been taken to mitigate risk.

Collaborate with EHR vendors. The EHR contains a lot of information that needs to be presented in helpful ways for practitioners to make decisions. Work with your EHR vendor and provide feedback to enhance the presentation of information and clinical decision-making based on your organization's needs.

A Carton Labeled Sildenafil Contained Tablets Labeled Buprenorphine!

An organization reported that they ordered buprenorphine 2 mg sublingual tablets (NDC: 60687-481-21), a controlled substance and partial opioid agonist, indicated for the treatment of opioid dependence. A pharmacy technician was adding the received product to inventory and identified that they were sent a carton labeled sildenafil 20 mg tablets (NDC: 60687-788-21) (**Figure 1**, page 4). However, the carton of the received product contained unit-dose blister packages labeled as buprenorphine 2 mg. The carton contained a total of 30 tablets (3 sheets with 10 tablets each). The products are made by American Health Packaging.

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organization purchases this product, notify staff of this issue. Develop order sets (e.g., for pulmonary embolism) and require prescribers to enter medication orders in the electronic health record (EHR) to maximize the benefit of clinical decision support and proactive pharmacist review. Use barcode scanning prior to administration, including in the ED. This event reminds us of two-component vaccine error reports where the diluent has been inadvertently administered without reconstituting the vaccine powder. Organizations should work with EHR vendors or internal developers to configure the system to enable (and require) scanning of both the alteplase powder and corresponding diluent barcodes during preparation and administration. If possible, include a pharmacist during code situations. Label all practitioner-prepared infusions and syringes, and read labels aloud prior to administration. When possible, have a second code team member independently check the dose and volume prior to administration and also share the source vial so that the drug and dose can be confirmed during the double check. Consider adding an auxiliary label to the carton to warn practitioners that the powder vial must be reconstituted with sterile water prior to administration. Report errors to ISMP.

Abbreviation Led to Vimpat Being Ordered Instead of Valproic Acid. An organization reported two close calls in which neurologists recommended "VPA" to ED providers verbally and in their consult notes for two different patients, intending to order valproic acid. In both cases, the ED providers misinterpreted VPA as **VIMPAT** (lacosamide) and prescribed the incorrect seizure medication. Pharmacists reviewing the orders identified the errors during verification because the prescribed dose did not align with typical Vimpat dosing, which prevented the wrong drug from reaching the patients.

The abbreviation VPA is ambiguous, as it may refer to valproic acid or be misinterpreted as part of the brand name Vimpat. The ISMP List of Error-Prone Abbreviations recommends practitioners avoid abbreviating drug names

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Figure 1. An organization ordered buprenorphine 2 mg sublingual tablets (left) and received a carton labeled sildenafil 20 mg tablets (right) that contained unit-dose blister packages labeled as buprenorphine.

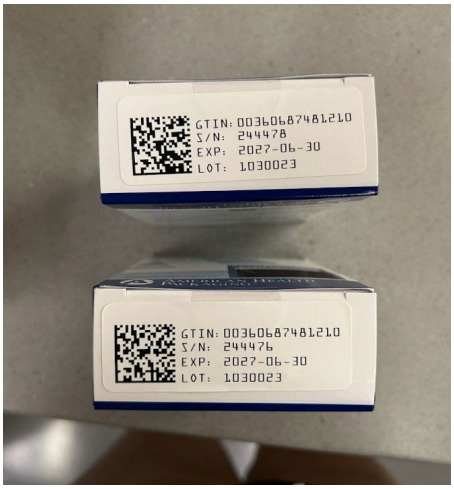

Figure 2. The carton labeled as sildenafil (top) and a carton labeled as buprenorphine (bottom) had the same expiration date and lot number.

The organization reported that the barcode on the carton labeled as sildenafil and the barcode on the tablets labeled as buprenorphine both scan as buprenorphine 2 mg. The sildenafil carton also had the same expiration date (6/30/2027) and lot number (1030023) as another carton labeled as buprenorphine (**Figure 2**). Thankfully, the organization only found one carton with this issue and caught the error prior to it reaching any patients.

We reached out to the US Food and Drug Administration (FDA) and American Health Packaging to report this concern. We asked American Health Packaging whether the tablets are buprenorphine or sildenafil, if other lots are impacted, and whether a formal recall is planned. They confirmed that the tablets within the blister packs are buprenorphine (**Figure 3**). They told us this is the first report about this batch related to an incorrect carton label and at this time, all indications suggest that this was an isolated incident. They did not have additional information but are actively investigating to determine the root cause and pervasiveness of the defect.

Figure 3. American Health Packaging confirmed that the tablets inside the carton labeled sildenafil are buprenorphine.

If your organization has purchased buprenorphine 2 mg sublingual tablets or sildenafil 20 mg tablets by American Health Packaging, immediately check your inventory in all locations. If impacted products are found, sequester them until further instructions are provided by the FDA and/or manufacturer. While barcode scanning is always an important step, notify staff that in this case the sildenafil carton may scan as buprenorphine. In addition to scanning, it is important to read the carton and blister package labels upon receipt in the pharmacy, prior to adding to storage, when refilling an automated dispensing cabinet (ADC), and before administration. Emphasize the need to be vigilant when checking American Health Packaging's buprenorphine and sildenafil tablets, regardless of the lot. Report issues to ISMP, FDA, and the manufacturer.

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entirely. Organizations should make it a policy and expectation to not use drug name abbreviations or acronyms when referring to medications and educate practitioners about how this could lead to an error. Coach staff to seek clarification of the full medication name whenever a practitioner uses an abbreviation or acronym, in both verbal and written communication. Always confirm that the dose and indication are consistent with the patient's clinical condition. Build order sets that include the drug's indication and maximize clinical decision support (e.g., dose range checking). Report close calls and errors due to abbreviations to ISMP.

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