

## Wrong-Time Error With High-Alert Medication

September 1, 2016

Yang A, Nelson LS. Wrong-Time Error With High-Alert Medication. PSNet [internet]. 2016.

<https://psnet.ahrq.gov/web-mm/wrong-time-error-high-alert-medication>

---

### The Case

A 60-year-old man was admitted to the hospital for a total knee arthroplasty. During the admission process in the early evening, the surgical resident restarted his maintenance home medications, including oral dofetilide (an antiarrhythmic agent) taken every 12 hours. In the electronic health record, drugs ordered for "q12 hour" dosing are scheduled for 6 AM and 6 PM by default. The overnight nurse saw that the morning dose was scheduled to be given at 6 AM, but the patient was scheduled to leave for the operating room before 6 AM, so she gave the dose early, at 4 AM. During his preoperative assessment at around 6 AM, the patient was noted to have severe QTc prolongation on his electrocardiogram, putting him at high risk for torsades de pointes, a sometimes fatal arrhythmia. Considering the acute ECG changes (prior QTc intervals were normal), surgery was canceled and the electrophysiology service was consulted.

The electrophysiology fellow felt that the 4 AM dofetilide administration likely contributed to the arrhythmia. Dofetilide is known to be associated with QTc prolongation if administered too early or at excessive doses. Further investigation revealed the patient also took his previous night's dose later than usual, at 10 PM. Consequently, rather than having received his dofetilide doses 12 hours apart, the 2 doses had been given only 6 hours apart. Neither the surgical resident nor the nurse responsible for administering the drug was aware of the risks associated with deviation from the strict 12-hour dosing interval, and neither had asked the patient about the timing of his last dofetilide dose.

The patient was monitored on telemetry for a few days, and surgery was delayed until the return of his QTc to baseline. After this case, the hospital added dofetilide to a list of drugs that could only be ordered by a specialty service.

### The Commentary

by Annie Yang, PharmD, and Lewis Nelson, MD

Although all medications carry risk of patient harm when used in error, some medications are riskier than others. These are known as high-alert medications. Dofetilide, an example high-alert medication, is an oral

Class III antiarrhythmic medication used for the conversion to and maintenance of normal sinus rhythm in patients with atrial fibrillation or atrial flutter. It can cause QTc prolongation in a dose-dependent manner. Therefore, increases in the plasma concentration of dofetilide—which may occur due to overdose, too frequent dosing, drug–drug interactions, or decreased renal function—elevates the risk of induced arrhythmias.(1) Considering the potential for serious adverse reactions, all hospitals should designate dofetilide as a high-alert medication.

National recommendations exist regarding designation of high-alert medications (e.g., Institute for Safe Medication Practice's [List of High-Alert Medications in Acute Care Settings](#)), but there is no national standard that hospitals are required to follow. Rather, The Joint Commission requires hospitals to develop their own high-alert medication list and to implement a process for managing these medications.(2) It is unknown whether the hospital in the current case had included dofetilide on its list. Even if they had, this case illustrates that simply identifying a medication as high-alert may not be enough to prevent errors from occurring.

### Preventing Harm With High-alert Medications in the Hospital Setting

While identification of high-alert medications is the first step to preventing harm, developing robust safeguards for their use is even more important. Without a detailed error-prevention plan implemented for each high-alert medication or medication class, creating a high-alert list does little more than meet a regulatory requirement. Some hospitals may rely solely on low-leverage, or relatively ineffective, risk reduction strategies such as high-alert labels on pharmacy bins or dispensed medications or double checks by nurses during administration.(3) However, these approaches may not adequately warn prescribers about a medication's high-risk designation. One strategy to ensure that error-prevention plans are comprehensive is to create safeguards in every node of the medication-use process. This strategy is used below to discuss the dofetilide case.

#### *Selection and procurement*

Most hospitals have an interdisciplinary committee, usually the Pharmacy and Therapeutics (P&T) Committee or the Drug and Formulary Committee, tasked with managing medication usage. While the primary role of the P&T committee is to manage the drug formulary, it must also be responsible for identifying medications that require special safeguards.(4,5) Dofetilide should have been identified as a high-alert medication by the P&T committee during the approval process. That designation should trigger the development of risk reduction strategies, which should be implemented before the medication is used at the institution. These strategies should be available in an institution-specific protocol readily accessible to practitioners.

#### *Prescribing*

Several strategies could be employed during the prescribing process. First, there should be a thorough medication reconciliation at all care transitions. At the time of admission, complete medication reconciliation should include documentation of the timing of the last dose, with subsequent timing based on that last dose's timing.(6) Prior to surgery, prescribers must weigh the risks and benefits of administering a patient's home medications, with a particular focus on high-alert medications. Considering the risks associated with

dofetilide, we believe that prescribing should be restricted to clinicians with appropriate expertise. The hospital instituted this restriction after the medication error in this case.

### *Order verification and dispensing*

Prospective pharmacist verification of medication orders is an important step in error prevention. For select high-alert medications, hospitals should delineate the parameters that a pharmacist should verify and document. For example, verification of a dofetilide order should include checking the patient's dose, renal function, QTc interval, time of the last administered dose, and concomitant medications (for drug–drug interactions). Some hospitals may not require prospective pharmacist verification of orders written in the perioperative setting, thus bypassing this safeguard. Finally, pharmacists should communicate any special administration instructions to nurses in the electronic medication administration record and/or on the medication label as part of the verification and dispensing process.

### *Administration*

Wrong-time errors are the most prevalent administration errors.<sup>(7,8)</sup> Although many wrong-time errors are benign, some medications require administration within a very narrow window to achieve the desired therapeutic result and/or to avoid adverse events. The Centers for Medicare and Medicaid Services (CMS) require that hospitals specify which medications are considered time-critical scheduled medications, those for which "an early or late administration of greater than thirty minutes might cause harm or have significant, negative impact on the intended therapeutic or pharmacological effect."<sup>(9)</sup> Medications requiring administration separate from other medications or certain designated premedications are examples. For non–time critical scheduled medications, the allowed administration window for a medication that is dosed twice-daily is one hour before or after the scheduled time.<sup>(9)</sup> The hospital's policy on timing of medication administration should be included in nursing orientation and education. Additionally, pertinent information should be available at the point of care as for time-critical scheduled medications. Many electronic health record (EHR) systems can alert a nurse attempting to administer a medication outside the acceptable administration window.

### *Monitoring*

All patients should be monitored for effectiveness and toxicity after administration of a medication. Prescribers and nurses should be aware of the signs and symptoms of both. In this case, the patient's QTc interval was measured as part of the preoperative assessment, but the surgeons and nurses may not have known that use of dofetilide mandates monitoring of the electrocardiogram for QTc prolongation. For medications with required monitoring parameters, EHR systems may be able to link medication and monitoring orders so that both are ordered simultaneously. Besides detailing monitoring parameters, medication orders should also specify subsequent actions to be taken (e.g., holding doses, discontinuing the medication).

### Preventing Harm With High-alert Medications Nationally: REMS

The FDA requires Risk Evaluation and Mitigation Strategies (REMS) from manufacturers as a safety strategy to manage a known or potential serious risk associated with certain medications.<sup>(10)</sup> The elements of an REMS can include medication guides to be dispensed to the patient. For providers and

health care systems, they also include Elements to Assure Safe Use, which may require prescribers to have specific training, pharmacies and practitioners to be certified, and patients to be enrolled in a registry.<sup>(11)</sup> Until recently, dofetilide was part of an REMS program that required the prescriber and hospital pharmacy to be certified and a medication guide be provided to the patient. Although there may no longer be FDA requirements for prescribing and dispensing of the medication, the risks associated with the drug still exist, and institution-specific risk reduction strategies should still be implemented.

#### Take-Home Points

- High-alert medications, those that bear a heightened risk of causing significant harm when inadvertently misused, warrant precautions at each node of the medication-use process.
- The risks associated with the medication and the safeguards to mitigate them should be known to patients, prescribers, pharmacists, and nurses.
- Certain medications are required by the FDA to have a Risk Evaluation and Mitigation Strategy, and all hospitals and practitioners must follow the outlined specific safety procedures.

Annie Yang, PharmD Assistant Director of Medication Safety and Quality NYU Langone Medical Center New York, New York

Lewis Nelson, MD Professor and Vice Chair for Academic Affairs Ronald O. Perelman Department of Emergency Medicine New York University School of Medicine Director, Fellowship in Medical Toxicology New York City Poison Control Center New York, New York

## References

1. Tikosyn [package insert]. New York, NY: Pfizer Inc; 2013.
2. 2015 Comprehensive Accreditation Manual for Hospitals. Oakbrook Terrace, IL: Joint Commission; January 2015 MM.01.01.03.
3. ISMP Medication Safety Alert! Acute Care Edition. Your high-alert medication list—relatively useless without associated risk-reduction strategies. April 4, 2013;18:1-5. [\[Available at\]](#)
4. Principles of a sound drug formulary system. Coalition Working Group; June 2000. [\[Available at\]](#)
5. Tyler LS, Cole SW, May JR, et al; ASHP Expert Panel on Formulary Management. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. Am J Health Syst Pharm. 2008;65:1272-1283. [\[go to PubMed\]](#)
6. Cohen MR. Preventing prescribing errors. In: Cohen MR, ed. Medication Errors. 2nd ed. Washington, DC: American Pharmacists Association;2006:175-202. ISBN: 9781582120927.
7. Barker KN, Flynn EA, Pepper GA, Bates DW, Mikeal RL. Medication errors observed in 36 health care facilities. Arch Intern Med. 2002;162:1897-1903. [\[go to PubMed\]](#)
8. Keers RN, Williams SD, Cooke J, Ashcroft DM. Prevalence and nature of medication administration errors in health care settings: a systematic review of direct observational evidence. Ann Pharmacother.

2013;47:237-256. [\[go to PubMed\]](#)

9. Revised hospital guidance for pharmaceutical services and expanded guidance related to compounding of medications. Baltimore, MD: Centers for Medicare & Medicaid Services (CMS). October 30, 2015.

[\[Available at\]](#)

10. Nelson LS, Loh M, Perrone J. Assuring safety of inherently unsafe medications: the FDA risk evaluation and mitigation strategies. J Med Toxicol. 2014;10:165-172. [\[go to PubMed\]](#)

11. FDA Basics Webinar: A Brief Overview of Risk Evaluation and Mitigation Strategies (REMS). Silver Spring, MD: US Food and Drug Administration. [\[Available at\]](#)

*This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. [View AHRQ Disclaimers](#)*