

## The Pharmacist's Role in Preventing Harm with Oral Anticoagulants



CELEBRATING  
10  
YEARS

### Faculty

**Matthew Grissinger, RPh, FISMP, FASCP**

Director, Error Reporting Programs  
Institute for Safe Medication Practices

Manager, Medication Safety Analysis  
PA Patient Safety Authority

### Disclosures

**Dr. Grissinger:** Employee (Spouse) – Johnson and Johnson

### Learning Objectives

- Describe errors and potentially hazardous situations associated with oral anticoagulants
- Evaluate the current trends in errors with the use of the newer oral anticoagulants
- Outline strategies for preventing anticoagulation errors using technology and other system changes
- Describe metrics that could be used to measure the level of patient harm with the use of oral anticoagulants

## History of Harm with Oral Anticoagulants

- One of the most commonly implicated drug classes in adverse drug events
- Most commonly implicated adverse drug events treated in US emergency departments and was responsible for 8% of all events
- Joint Commission NPSG 03.05.01 established 2008
- Retrospective, hospital-specific, 5-year study found that 48.8% (n=226) of all anticoagulant-associated adverse drug events involved medication errors

Office of Inspector General (OIG), US Department of Health and Human Services [website]. <http://oig.hhs.gov/oel/reports/oel-06-09-00090.pdf>. Accessed February 6, 2018. Budnitz DS, et al. JAMA. 2006;296:1858-1866. Joint Commission [website]. [https://www.jointcommission.org/assets/1/6/NPSG\\_Chapter\\_HAP\\_Jan2017.pdf](https://www.jointcommission.org/assets/1/6/NPSG_Chapter_HAP_Jan2017.pdf). Accessed February 6, 2018. Piazza G, et al. Am J Med. 2011;124(12):1136-1342.

## Ten Key Elements of Medication Use System

1. Patient information
2. Drug information
3. Communication of drug information
4. Labeling, packaging, and nomenclature
5. Drug storage, stock, standardization, and distribution
6. Device, acquisition, use, and monitoring
7. Environmental factors
8. Staff competency and education
9. Patient education
10. Quality and risk management issues

Institute for Safe Medication Practices [website]. [www.ismp.org/faq.asp#Question\\_3](http://www.ismp.org/faq.asp#Question_3). Accessed February 6, 2018.

## Patient Information

- **Lack of critical patient information**
  - Laboratory values
  - Weight
  - Diagnoses
  - Allergies
  - Other drug therapy
  - Order entry systems that do not use relevant patient information

## Patient Information Problems

- **Renal impairment**
  - Failure to reduce dose in patients with decreased renal function
- **Laboratory values**
  - Failure to verify laboratory values before prescribing or administering
  - Too frequent dose adjustments without assessing upward or downward trend in INR values

INR = international normalized ratio.

## Patient Information Problems

### • Duplicate or concurrent therapy

- LMWH given in ED and heparin infusion started too soon on inpatient care unit
- Concomitant use of warfarin and other antithrombotics

### • Patient weight

- Estimated or not verified
- Mix-ups between pounds and kilograms

ED = emergency department; LMWH = low-molecular-weight heparin.

## Medication Errors Associated with Wrong Patient Weights

Top Medications Involved in Wrong-Weight Medication Error Reports (n=304)

Medication	Total
Heparin sodium*	110
Enoxaparin (Lovenox®)*	84
Acetaminophen (Tylenol®)	20
Dobutamine*	17
Dopamine*	17
Gentamicin sulfate	17
Vancomycin	14
Ibuprofen (Motrin®)	9
Nesiritide (Natrecor®)	8
Propofol (Diprivan®)*	8

\*High-alert medications.  
Pennsylvania Patient Safety Authority [website]. [http://patientsafety.pa.gov/ADVISORIES/Pages/200903\\_10.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/200903_10.aspx). Accessed February 6, 2018.

## Medication Errors Associated with Wrong Patient Weights

Types of Errors Involving Wrong Weight (n=479)

Categories	Total	% of Total Reports
Confusion between pounds vs kilograms	129	26.9
Documented weight was too high	83	17.3
Documented weight was too low	48	10
No weight was available or used	45	9.4
Incorrect estimated weight	17	3.5
Mix-up between ideal vs actual weight	11	2.3
Calculation error	6	1.3
Mix-up between height/temperature vs weight	4	0.8
Others	10	2.1
Unknown*	126	26.3

\*There was not enough information mentioned in the report to determine what went wrong.  
Pennsylvania Patient Safety Authority [website]. [http://patientsafety.pa.gov/ADVISORIES/Pages/200903\\_10.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/200903_10.aspx). Accessed February 6, 2018.

## Communication of Drug Information Involving Oral Anticoagulants

- Confusing directions (alternate-day dosing)
- Changes in directions via telephone, which cause confusion for patients
- Failure to take recent prescribing of vitamin K into consideration when resuming therapy
- Automatic stop orders
- Failure to hold pre-procedure
- Failure to resume orders post-procedure
- Confusion with name

## Faxed Order for...

~~Heparin~~  
 Heparin 18000U  
 LU 180 CP#05214 SQ 0.5 mL  
 Syringes 1cc 30 g/1.5  
 100

Institute for Safe Medication Practices [website]. <https://www.ismp.org/newsletters/acutecare/issue.aspx?id=20>. Accessed February 6, 2018.

## Dalteparin, Not Heparin

NOM NAME \_\_\_\_\_  
~~Heparin~~  
 → dalteparin 18000U  
 LU 180 CP#05214 SQ 0.5 mL  
 30 g/1.5

Institute for Safe Medication Practices [website]. <https://www.ismp.org/newsletters/acutecare/issue.aspx?id=20>. Accessed February 6, 2018.

1 ~~D. curvulinus~~ 8 mg  
 PO daily

2 Curvulinus Drug  
 disp: #90  
 Sig: PO daily

3 All previous curvulinus orders  
curvulinus 2 mg p.o. b.i.d.  
curvulinus 4 mg p.o. q.a.m.

## REVIEWS & ANALYSIS

### Oral Anticoagulants: A Review of Common Errors and Risk Reduction Strategies

Joseph Andrews, MD, PharmD  
 Medicine (Geriatrics), VA, PhD, RACP  
 Manager, Medication Safety, American  
 Pharmaceutical Research Society, Australia

#### ABSTRACT

Oral anticoagulants, a class of high-alert medications, are widely used in the United States for various indications, including treatment of acute or subacute venous thromboembolism and pulmonary embolism as well as prevention of stroke in atrial fibrillation. Analysis of adverse medication events reported from July 2013 through June 2014 through the National Patient Safety Reporting System (NPSRS) involving four oral anticoagulants—warfarin, dabigatran, rivaroxaban, and apixiban. Of the 421 events related to oral anticoagulants, 32 (8%) were related to warfarin, 15 (4%) to dabigatran, 11 (3%) to rivaroxaban, and 1 (0.2%) to apixiban. The most common errors were related to warfarin (32/421, 7.6%), followed by dabigatran (15/421, 3.6%), rivaroxaban (11/421, 2.6%), and apixiban (1/421, 0.2%). The most common errors were related to warfarin (32/421, 7.6%), followed by dabigatran (15/421, 3.6%), rivaroxaban (11/421, 2.6%), and apixiban (1/421, 0.2%). The most common errors were related to warfarin (32/421, 7.6%), followed by dabigatran (15/421, 3.6%), rivaroxaban (11/421, 2.6%), and apixiban (1/421, 0.2%).

Corresponding Author  
 Andrew Andrews

#### INTRODUCTION

Oral anticoagulants have been identified as one of the most commonly implicated drug classes in adverse drug events.<sup>1</sup> In fact, anticoagulation and cardiovascular agents, when compared with other medications, are more likely to cause potentially preventable adverse events due to medication errors.<sup>2</sup>

The Institute for Safe Medication Practices (ISMP) monitors and investigates medication errors, and has been a long-standing advocate for the use of anticoagulants, such as dabigatran or rivaroxaban, to reduce the risk of bleeding events during treatment of venous thromboembolism (VTE) and stroke prevention in atrial fibrillation (AF).<sup>3</sup> The Institute for Safe Medication Practices (ISMP) has been a long-standing advocate for the use of anticoagulants, such as dabigatran or rivaroxaban, to reduce the risk of bleeding events during treatment of venous thromboembolism (VTE) and stroke prevention in atrial fibrillation (AF).<sup>3</sup>

In a systematic, longitudinal, 6-year study by Fries et al.,<sup>4</sup> the investigators found that 40.9% (n = 120) of all adverse drug events involved anticoagulation medications. In the study, the 30-day mortality rate was increased in the 12% of patients who experienced an anticoagulation-related adverse drug event. Anticoagulation medications were the most common cause of adverse drug events in the study. The most common errors were related to warfarin (32/421, 7.6%), followed by dabigatran (15/421, 3.6%), rivaroxaban (11/421, 2.6%), and apixiban (1/421, 0.2%).

Warfarin, a vitamin K antagonist, works by altering the synthesis of vitamin K-dependent clotting factors II, VII, IX, and X. Dabigatran and rivaroxaban, direct thrombin inhibitors, work by inhibiting prothrombin activation and thus the formation of fibrin and insoluble clots. Rivaroxaban, a factor Xa inhibitor, works by directly inhibiting both the prothrombin and fibrinogen pathways, resulting in reduced thrombin and fibrin formation.

Unlike warfarin, dabigatran and rivaroxaban cannot be monitored using standard coagulation tests (PT/INR) or other blood tests and do not require dosage adjustments.<sup>5</sup> Although all anticoagulants are effective in the treatment of VTE, dabigatran and rivaroxaban have been shown to be superior to warfarin in terms of efficacy and safety in the treatment of VTE.

Andraica I, et al.  
 Pa Patient Saf Advis. 2015;12(2):54-61.

## Most Common Types of Events

Number of Oral-Anticoagulant-Related Medical Errors, by Event Type,  
Reported to the Pennsylvania Patient Safety Authority, July 2013 through June 2014 (N=831)

Event Type	n	%
Dose omission	270	32.5
Other (specify)	154	18.5
Extra dose	97	11.7
Wrong dose/overdosage	50	6.0
Monitoring error: clinical (lab value, vital sign)	46	5.5
Wrong time	40	4.8
Unauthorized drug	34	4.1
Wrong dose/underdosage	28	3.4
Wrong patient	23	2.8
Medication list incorrect	22	2.6

Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

## Errors with Oral Anticoagulants

- Medical-surgical units had the highest incidence of **reported** errors at 24.1% (n=200), followed by telemetry at 9.9% (n=82), and then rehabilitation units with 9.4% (n=78)
- Warfarin was predominantly reported (81.5%, n=677), followed by rivaroxaban (11.9%, n=99), dabigatran (3.6%, n=30), and apixaban (2.2%, n=18)
- 78.7% (n=654) of errors involved adults aged 60 years or older
  - More than one-third (34.4%, n=286) involved adults aged 80 years or older
- Nearly one-third of cases (29.4%, n=244) were reported as having an NCC MERP harm score of D to F

Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61. National Coordinating Council for Medication Error Reporting and Prevention [website]. [www.nccmerp.org/types-medication-errors](http://www.nccmerp.org/types-medication-errors). Accessed February 6, 2018.

## Dose Omissions

- Risk of a thromboembolic event
- Reasons varied
  - Medication not being ordered (eg, warfarin)
  - Orders not being administered (eg, orders "held" or transitions of care)
  - Orders being processed incorrectly (eg, system defaults)

Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

## Extra-Dose Errors

- Increased risk of bleeding events
- Reasons
  - Not "holding" warfarin after elevated INR
  - Change in clinicians
  - Communication errors
  - Patient's MAR not thoroughly reviewed

MAR = medication administration record.  
Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

## Error Type “Other”

- Prescribing errors (29.2%, n=45)
  - Primarily involved duplication of therapy
  - “Bridging”
- Incomplete medication list (13.0%, n=20)
  - Particularly during transitions of care

Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

## Duplication of Therapy

*“The patient was receiving heparin 5000 units [subcutaneously] every 8 hours for DVT prophylaxis.*

*Later in the day, apixaban 5 mg BID was also prescribed. The heparin was **not** discontinued.*

*Therefore, the patient received subcutaneous heparin while receiving therapeutic anticoagulation with apixaban.”*

DVT = deep vein thrombosis.  
Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

## Anticoagulation Bridging

*“Physician wrote orders for dabigatran, subcutaneous Lovenox,<sup>®</sup> and warfarin. The medications were not administered, and all orders were discontinued by the physician except for the Lovenox.”*

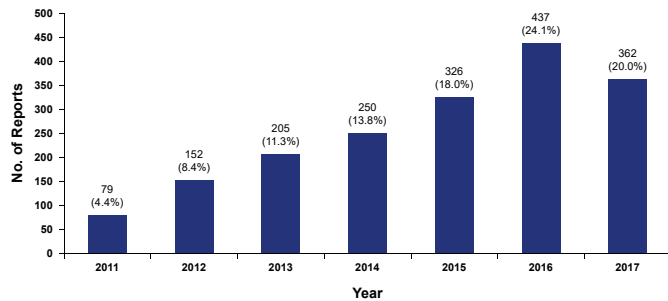
Andreica I, et al. *Pa Patient Saf Advis.* 2015;12(2):54-61.

The screenshot shows the Patient Safety Authority (PSA) website. The main content area displays a document titled "Identifying Patient Harm from Direct Oral Anticoagulants" dated June 15, 2018. The document is categorized under "Patient Safety Topics" and "Advisories & Events". It includes an abstract and an introduction section. The abstract discusses the PSA's database of events involving DOACs from January 2011 through August 2017, highlighting that 1,611 reported events, including 265 that resulted in patient harm, were analyzed. The introduction mentions that about 2.6 million people have atrial fibrillation in the United States, and that the number is expected to rise to 12 million by the year 2050.

Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

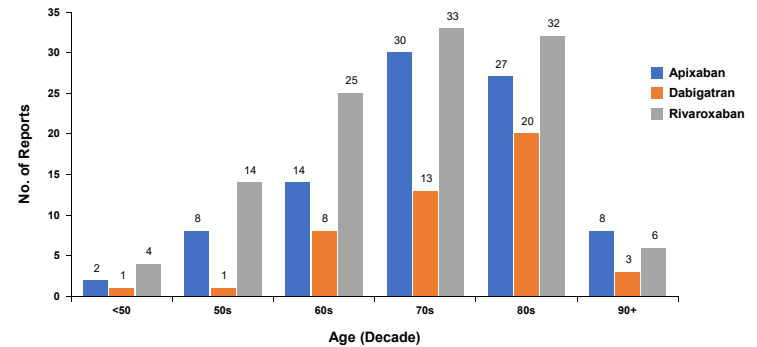
## Review of Adverse Drug Events Involving Direct Oral Anticoagulants

Number of Events Involving Direct Oral Anticoagulants by Event Year (N=1811)



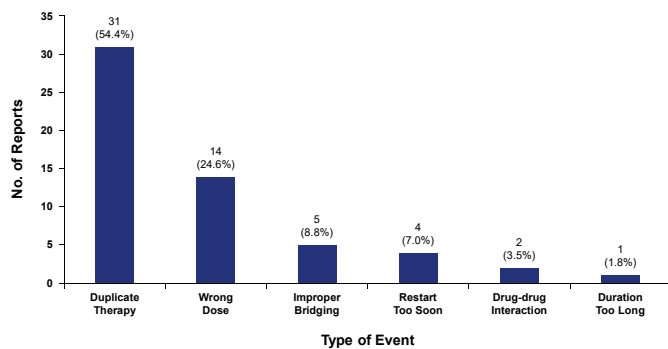
Note: Data reported through the Pennsylvania Patient Safety Reporting System, January 2011 through August 2017.

## Adverse Events Involving Direct Oral Anticoagulants by Decade of Patient Age (N=249)



Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Types of Preventable Adverse Events Involving Direct Oral Anticoagulants (N=57)



Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Example of Duplicate Therapy

- 78-year-old patient had hip surgery in the fall and has not been as mobile since. She has recently started ambulating
- She presented to the ED [emergency department] with left lower extremity swelling and pain and was diagnosed with a DVT
- The ED physician wrote for Lovenox [enoxaparin] 130 mg subcutaneously and decided to admit the patient to the hospital
- The inpatient physician came to see the patient and prescribed Xarelto [rivaroxaban] 15 mg 2 hours after the Lovenox [enoxaparin] was administered
- The patient had a significant gastrointestinal bleed 24 hours after the duplicate therapy was administered. The patient went into shock and was transferred to the ICU [intensive care unit]. The patient was given factor IX, fresh frozen plasma, and packed red blood cells

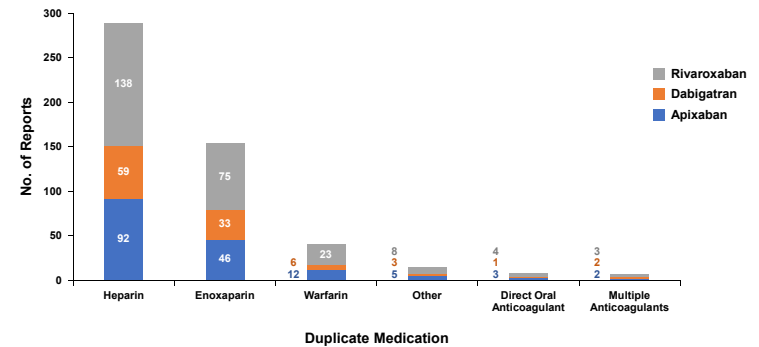
Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Examples of Bridging Errors

- 87-year-old male patient received warfarin. Dabigatran was started as a "bridge to Coumadin therapy." Patient transferred to ICU. Patient developed bilateral nasal bleeding. Received vitamin K, fresh frozen plasma, and packed RBCs. The aPTT [activated partial thromboplastin time] result was elevated
- 92-year-old female patient admitted with hydropneumothorax. Had been taking apixaban 2.5 mg bid [twice a day] at home, and this was resumed [on the fourth day of the admission]. [Four days later] she was also started on warfarin 5 mg with plan to continue apixaban x 3 doses as bridge. [The next day the patient] was noted to have hematuria, INR = 1.6. Apixaban was discontinued and warfarin was continued. INR [the next day] was 1.7 with no additional bleeding documented

Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Medications Involved in Therapeutic Duplication Errors without Harm (N=515)



Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Effects on Procedure Cancellations

- Outpatient procedure cancellations and complications due to patients either holding or not holding their direct oral anticoagulants were noted in 7.6% (n=137 of 1811) of reports
- In 88.3% (n=121 of 137) of those reports, the procedure was canceled when the direct oral anticoagulant had not been held

Valentine D, et al. Identifying Patient Harm from Direct Oral Anticoagulants. *Pa Patient Saf Advis.* 2018 Jun;15(2). [http://patientsafety.pa.gov/ADVISORIES/Pages/201806\\_DOACs.aspx](http://patientsafety.pa.gov/ADVISORIES/Pages/201806_DOACs.aspx). Accessed July 16, 2018.

## Risk-Reduction Strategies

- Focus on system-based causes
  - Constraints
  - Standardization
  - Redundancies
  - Education and information
  - Monitoring of adverse drug events



## Constraints

- A pharmacist's review prior to dispensing
  - No overrides!
- Functional drug alerts (eg, hard stops)
- Elimination of verbal orders
- "Read-back" method in case of emergency verbal order

Andreica I, et al. *Pa Patient Saf Advis*. 2015;12(2):54-61.

## Standardization

- Prescribing
  - Required baseline information
  - Updating computer systems and healthcare records
  - "Hold" orders
  - Anticoagulation management service (AMS) programs for dosing, monitoring, and teaching patients
  - Rapid or emergency reversal of anticoagulation
  - Incomplete or "blank" orders
  - "NOAC"

Institute for Safe Medication Practices [website]. [www.ismp.org/Newsletters/acutecare/articles/20070111.asp](http://www.ismp.org/Newsletters/acutecare/articles/20070111.asp). Accessed February 6, 2018.

## Standardization

- Dispensing and administration
  - Administer warfarin at standard time
  - Eliminate limited selection of medications in the formulary, if possible
  - Define policies and procedures for therapeutic substitution or ways to approve use of a patient's own medication

Pharmacy Times [website]. <http://www.pharmacytimes.com/publications/health-system-edition/2013/july2013/new-oral-anticoagulants-implications-for-health-systems>. Accessed February 6, 2018.

## Redundancies

- Strategically placed, independent double checks
- Clinical decision support in computerized order entry
- Bar-code scanning

Institute for Safe Medication Practices [website]. [www.ismp.org/Newsletters/acutecare/articles/20070111.asp](http://www.ismp.org/Newsletters/acutecare/articles/20070111.asp). Accessed February 6, 2018.

## Therapeutic Monitoring

- Baseline laboratory test results need to be available in a timely manner
- Process control charts
  - To display trends of daily INR values

Institute for Safe Medication Practices [website]. [www.ismp.org/Newsletters/acute/articles/20070111.asp](http://www.ismp.org/Newsletters/acute/articles/20070111.asp). Accessed February 6, 2018.

## Education and Information

### • Staff

- Annual competence assessments
- New anticoagulant in the organization's formulary
- Underlying protocol (such as reversal protocols)
- Expertise in therapy management

### • Patient

- Remind patients that the risks of anticoagulants include bleeding
- Patient's ability to afford and purchase the medicine
- Provide education a couple days prior to discharge

Institute for Safe Medication Practices [website]. [www.ismp.org/Newsletters/acute/articles/20070111.asp](http://www.ismp.org/Newsletters/acute/articles/20070111.asp). Accessed February 6, 2018.

## Monitoring of Adverse Drug Events

- Adverse drug event triggers
  - INR >6
  - Bleeding
  - Administration of reversal agents

Adverse Drug Event Trigger Tool. Centers for Medicare & Medicaid Services (CMS). <https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/QAPI/Downloads/Adverse-Drug-Event-Trigger-Tool.pdf>.

## Free Tools to Address Anticoagulants



Institute for Safe Medication Practices [website]. [www.ismp.org](http://www.ismp.org). Accessed February 6, 2018.

## Conclusions

- Oral anticoagulants are considered high-alert medications
- Complexity of the target-specific agents introduces more opportunities for errors
- Effective risk-reduction strategies will help hospitals minimize the occurrence of preventable oral-anticoagulant-related adverse events

Questions?