

2013

Medication Utilization Evaluation of Dabigatran and Rivaroxaban within a Large, Multicenter Health System.

Sarah A. Nisly

Butler University, snisly@butler.edu

Alex N. Issacs

Indiana University Health

Meagan Doolin

Butler University

Courtney Morse

Butler University

Erin Shiltz

Indiana University Health

Follow this and additional works at: http://digitalcommons.butler.edu/cophs_papers



Part of the [Pharmacy Administration, Policy and Regulation Commons](#)

Recommended Citation

Nisly, Sarah A.; Issacs, Alex N.; Doolin, Meagan; Morse, Courtney; and Shiltz, Erin, "Medication Utilization Evaluation of Dabigatran and Rivaroxaban within a Large, Multicenter Health System." (2013). *Scholarship and Professional Work – COPHS*. 31.

http://digitalcommons.butler.edu/cophs_papers/31

This Article is brought to you for free and open access by the College of Pharmacy & Health Sciences at Digital Commons @ Butler University. It has been accepted for inclusion in Scholarship and Professional Work – COPHS by an authorized administrator of Digital Commons @ Butler University. For more information, please contact omacisaa@butler.edu.

Medication Utilization Evaluation of Dabigatran and Rivaroxaban within a Large, Multi-Center Health System

Alex N. Isaacs, Pharm.D., BCPS^{1,2}; Meagan Doolin, Pharm.D. Candidate²; Courtney Morse, Pharm.D. Candidate²; Erin Shiltz, Pharm.D., BCPS³; Sarah A. Nisly, Pharm.D., BCPS^{2,3}

1) PGY-2 Pharmacotherapy Resident, Indiana University Health, Indianapolis, IN 2) Butler University College of Pharmacy and Health Sciences, Indianapolis, IN 3) Clinical Pharmacy Specialist – Internal Medicine, Indiana University Health, Indianapolis, IN

Abstract

Objective. The objective of this medication utilization evaluation (MUE) was to determine the appropriateness of dabigatran and rivaroxaban while also reviewing outcomes for safety and effectiveness within a large, multi-center health system.

Methods. A retrospective chart review was performed using the system's electronic medical record. A data inquiry was requested and generated for dabigatran usage from July 28, 2011 through July 28, 2012 and for rivaroxaban from March 1, 2012 to July 31, 2012 at eight health system hospitals. All patients receiving at least one dose were eligible for inclusion in the MUE.

Results. For dabigatran, 78 of 390 unique patient encounters were analyzed (20%). All 62 rivaroxaban encounters were included in the analysis. Dabigatran was used for appropriate indications in 94% of encounters and 82% for rivaroxaban. Based on indication and renal function, 87% of dabigatran patients and 92% of rivaroxaban patients received correct dosing. For patients transitioning to or from another anticoagulant, appropriate transitions occurred in 44% of dabigatran transitions and 48% of rivaroxaban transitions. At discharge, 83% of dabigatran and 86% of rivaroxaban therapy was continued. There were no reported strokes or systemic embolism with dabigatran, but one reported deep vein thrombosis occurred during hospitalization with rivaroxaban therapy. Documented bleeds in 5% of dabigatran and 3% of rivaroxaban patients. Patient education was documented for 37% of dabigatran and 26% of rivaroxaban patients receiving therapeutic anticoagulation.

Conclusion. This MUE revealed the appropriate use of dabigatran and rivaroxaban therapy with few safety outcomes within a large, multi-center health system.

Introduction

New oral anticoagulants have created excitement as potential replacements for warfarin therapy in the treatment and prevention of thromboembolism. In 2010, dabigatran etexilate (Pradaxa[®]), an oral direct thrombin inhibitor, received Federal Drug Administration (FDA) approval for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation.¹ In 2011, rivaroxaban (Xarelto[®]) was FDA approved as the first oral factor Xa inhibitor for the reduction of stroke and systemic embolism in patients with non-valvular atrial fibrillation and for post-operative venous thromboembolism (VTE) prophylaxis in patients undergoing knee and hip replacement surgery.² Additionally, in 2012, rivaroxaban received FDA approval for the treatment of deep-vein thrombosis (DVT) and pulmonary embolism (PE).³ The new oral anticoagulants are appealing alternatives to current standard therapy, with demonstrated non-inferiority for thromboembolic indications and less stringent monitoring.⁴⁻¹¹

The efficacy of dabigatran was demonstrated in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial comparing dabigatran against warfarin in the prevention of stroke and systemic embolism in non-valvular atrial fibrillation. Dabigatran 150 mg by mouth twice daily was superior to warfarin therapy in reduction of stroke and systemic embolism, but the incidence of major bleeding was similar.⁴ Rivaroxaban demonstrated non-inferiority to warfarin in the reduction of stroke and systemic embolism in patients with non-valvular atrial fibrillation in the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF).⁵ For VTE prophylaxis, as shown in the Regulation of Coagulation in Orthopedic Surgery to Prevent Deep Venous Thrombosis and Pulmonary Embolism (RECORD) trials, rivaroxaban illustrated superiority over enoxaparin in the prevention of DVT, PE, and mortality in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA).⁶⁻⁹ The

Alex Isaacs was PGY-2 Pharmacotherapy Resident at Indiana University Health and Butler University College of Pharmacy and Health Sciences in Indianapolis, IN at the time this research was conducted. Email correspondence: aisaacs1@iuhealth.org. The authors disclose no conflicts of interest.

EINSTEIN investigators exemplified rivaroxaban non-inferiority to warfarin for the initial and continued treatment of DVT and PE events with similar bleeding risks.^{10,11} The manufacturer recommended dosing for approved indications is listed in Table 1.^{1,2}

With the advent of these new agents, transitions between anticoagulants hold the potential for serious medication errors. Appropriate transitions between agents are essential to optimize care and reduce morbidity and mortality. Conversion to or from dabigatran or rivaroxaban requires monitoring and caution is necessary to minimize thromboembolic and bleeding complications. Table 1 provides the manufacturer recommended transitions between available anticoagulants.^{1,2}

Lastly, while both dabigatran and rivaroxaban have shown efficacy in reducing the risk of systemic thromboembolism, potential side effects, including bleeding, are an inherent risk with these medications. The Adverse Events Reporting System (AERS) database has noted bleeding as a commonly reported complication with dabigatran and rivaroxaban therapy.^{12,13}

Dabigatran and rivaroxaban were added to the Indiana University Health system formulary with order set development on March 1, 2011 and March 1, 2012, respectively. Upon addition to the formulary, both medications required a mandatory order set to initiate therapy due to the inherent risks associated with anticoagulant therapy. A medication utilization evaluation (MUE) was performed at eight hospitals within the large multi-center health system. The primary objective of this MUE was to determine the appropriateness of dabigatran and rivaroxaban use while also reviewing potential outcomes for safety and effectiveness within a large, multi-center health system.

Methods

A retrospective chart review was performed using the system's electronic medical record (EMR). A data inquiry was requested and generated for dabigatran usage from July 28, 2011 through July 28, 2012 and for rivaroxaban from March 1, 2012 to July 31, 2012 at eight IUH hospitals. Search terms for the inquiry included "dabigatran", "Pradaxa[®]", "rivaroxaban", and "Xarelto[®]." All dosage strengths for each anticoagulant were included in this chart review. Patients receiving at least one dose during their hospital stay were eligible for inclusion. An online random number generator was used to select dabigatran encounters for review. IRB approval was obtained from Indiana University.

Data extracted from the EMR included patient demographics (age, weight, and baseline renal function), indication, utilization prior to admission, inpatient dosage strength, number of doses administered, appropriateness of dose, assessment for appropriate monitoring of laboratory data, transitioning between anticoagulants, discharge regimen, reason for discontinuation, documented thromboembolism or bleeding, and documentation of anticoagulant education. The indication for use was collected from provider clinical notes and was evaluated for appropriateness based on FDA approved indications at the time of the study period. Utilization prior to admission was gathered from the admission note or admission medication history. The inpatient dose was defined as the dose most frequently received by the patient during hospitalization. Doses were evaluated as appropriate based on renal function and manufacturer recommended dosing for prophylactic or therapeutic indications. Specific reasons for discontinuation, documented bleeding, and thromboembolic events were collected from practitioners' clinical notes in the EMR.

Based on system protocols, appropriate monitoring was defined as baseline hemoglobin and at least once weekly and serum creatinine at baseline and at least every four days. Serum creatinine was used to assess renal function by calculation of the creatinine clearance (CrCl) utilizing the Cockcroft-Gault equation. Dosing was considered appropriate based on the dosing adjustments recommended by the manufacturers in Table 1. Transitional therapy between anticoagulants was evaluated utilizing the electronically reported medication administration times documented by nursing staff. Transitions were determined appropriate and inappropriate utilizing manufacturer recommended transitions (Table 1).^{1,2} Concomitant administration of antiplatelet agents was not considered duplicate anticoagulation. Statistical analysis was performed using descriptive statistics.

Results

The data query produced 390 dabigatran orders with 20% (n=78) encounters analyzed. The query resulted in 62 rivaroxaban encounters and all rivaroxaban patient data was reviewed (n=62). Baseline characteristics are listed in Table 2.

When assessing use prior to hospital admission, 62% (n=48) of dabigatran patients and 24% (n=15) of rivaroxaban patients were receiving the medication as an outpatient. According to package labeling at the time of the study, use for appropriate indications occurred in 94%

(n=73) of dabigatran and in 82% (n=51) of rivaroxaban encounters. Indications for use of dabigatran and rivaroxaban are shown in Table 3. It is worth noting that, 38% of the off-label uses during hospitalization were continuation of home therapy occurring in four of five dabigatran and two of eleven rivaroxaban encounters.

Information on inpatient dosing is provided in Table 4. Based on indication along with renal function, 87% (n=68) of dabigatran patients and 92% (n=57) of rivaroxaban patients received correct dosing per the manufacturer.^{1,2} Continuation of home doses occurred in 60% (n=9) of the incorrect dosing encounters with seven out of ten incorrect for dabigatran and two out of five for rivaroxaban. Inappropriate renal adjustment was the cause of all incorrect dabigatran doses and 80% (n=4) of incorrect rivaroxaban dosing encounters. Appropriate hemoglobin and serum creatinine monitoring occurred in 97% (n=76) of dabigatran encounters and 87% (n=54) for rivaroxaban.

While the dosing was appropriate for a majority of patients, there were concerns with the transitions between the new oral anticoagulants and conventional anticoagulants (Figure 1). For dabigatran, transitioning to or from another anticoagulant occurred in 46% (n=36) of patients with only 44% (n=16) appropriate.¹ There were 37% of encounters (n=23) in which patients were transitioned between another anticoagulant and rivaroxaban. Of the 23, there were 48% (n=11) with correct transitions as recommended by the manufacturer.²

At discharge, 83% (n=65) of dabigatran and 86% (n=53) of rivaroxaban therapy was continued. For patients being discharged on dabigatran, 94% (n=61) had dabigatran prescribed for an FDA approved indication and 91% (n=59) had correct dosing based on indication and renal function. Rivaroxaban patients upon discharge had an FDA approved indication in 85% of encounters (n=45) and 94% (n=50) had correct dosing based on indication and renal function.

For patients with therapy discontinued prior to discharge, reasons included: transitioning to other anticoagulants, worsening renal function, death, thromboembolic and bleeding complications, and completion of anticoagulant therapy. There were no reported strokes or systemic embolism in patients receiving dabigatran. There was one death in a patient receiving dabigatran, but the death was contributed to pulmonary complications unrelated to dabigatran therapy. One VTE occurred during hospitalization in patients receiving rivaroxaban therapy. Bleeding resulted in the discontinuation of therapy in three dabigatran and one

rivaroxaban patients, but there were documented bleeds in 5% (n=4) of dabigatran patients and 3% (n=2) of rivaroxaban patients. Patient education prior to discharge was performed for 37% (n=29) of dabigatran encounters and 26% (n=8) of rivaroxaban patients receiving therapeutic doses.

Discussion

With any new medication release, post-marketing surveillance is crucial to evaluate its use within clinical practice along with potential safety and effectiveness outcomes. The recent Anticoagulation Forum consensus statement recommends monitoring of quality indicators to assess patient outcomes and identify areas for improvement.¹⁴ Due to the intrinsic bleeding risks and potential for thromboembolic events, the new oral anticoagulants must be assessed in a clinical setting. This combined MUE for dabigatran and rivaroxaban reviewed the utilization of these new oral anticoagulants within a large, multi-center health system.

Overall, dabigatran and rivaroxaban therapy were prescribed and dosed appropriately in the majority of patients. These anticoagulants were used for FDA approved indications in 89% of encounters. It is worth noting that during the study period, rivaroxaban had not yet received FDA indication for the treatment of DVT or PE. Treatment with rivaroxaban for these indications was deemed inappropriate for this MUE. Additionally, similar safety profiles were revealed for dabigatran and rivaroxaban, when compared to larger clinical trials.⁴⁻¹¹ Non-major bleeding complications occurred in 5% of non-valvular atrial fibrillation patients on dabigatran, less than the 30% of patients who reported major or minor bleeding in the RE-LY trial.⁴ Rivaroxaban bleeding occurred in 3.2% of patients in this study, with one patient status post TKA and the other with atrial fibrillation. This is comparable to the 3.3-6.6% of combined major and minor bleeding in the RECORD trials and less than the 14.9% seen in the ROCKET-AF.⁵⁻⁹ Bleeding complications were likely lower than reported in clinical trials due to the retrospective surveillance used in this chart review, as compared to extensive observation during the RE-LY and ROCKET-AF trials.

Excluding bleeding events, few other complications occurred in patients evaluated for this MUE. There was one documented death for a patient receiving dabigatran, but this was contributed to pulmonary complications unrelated to dabigatran use. There were no reports of stroke or systemic embolism during hospitalization in the dabigatran arm and one

report of a post-operative DVT in a patient receiving prophylactic rivaroxaban. This encounter led to a similar VTE rate, when compared to the incidence in the four RECORD trials (3.6% vs. 1-10% respectively).⁶⁻⁹

Appropriate transitions between anticoagulant therapies are imperative to reduce the risk of thromboembolism and bleeding and this MUE revealed concerns in transitioning between anticoagulants. While delays in therapy during a transition between agents occurred with both anticoagulants, no delays resulted in a thromboembolism. Inappropriate transitions from this MUE revealed dual anticoagulants and administration of new anticoagulants too soon after discontinuation of previous therapy, enhancing the bleeding risk. This was demonstrated as one of the rivaroxaban minor bleeds occurred in a patient where rivaroxaban therapy was initiated six hours after receiving enoxaparin. Since practitioners often have less experience with these new anticoagulants, it is vital to educate on proper transitions between anticoagulants to enhance the safety and effectiveness of dabigatran and rivaroxaban.

Finally, due to potential bleeding and thromboembolic complications inherent with all anticoagulants, patient counseling is imperative. The overall rate of anticoagulation patient education for therapeutic indications for both anticoagulants was only 34% in this MUE. The Joint Commission recommends patient education for all therapeutic anticoagulants prior to discharge.¹⁴ Additionally, the Anticoagulation Forum stresses the importance of patient education counseling to enhance the safe and effective use of these anticoagulants in the post-discharge process.¹⁵ Patient education in the hospital setting is vital to ensure appropriate utilization and understanding of these medications. Educational instructions may include proper medication administration, compliance, monitoring, drug and food interactions, and potential adverse reactions from anticoagulant therapy. Patient education continues to be a focus for pharmacists to ensure patients are adequately informed of their therapy, potentially minimizing thromboembolic and bleeding complications.

This MUE is the first to evaluate the use of these medications within a large, multi-center health system; however, it is not without limitations. Due to the large number of patients receiving dabigatran, encounters were randomly selected and not all patients who received doses were reviewed in this analysis. Patients were only considered for inclusion if they had an order for dabigatran or rivaroxaban. Therefore, all bleeding and thromboembolic complications may not have been

evaluated as there could have been patients who had the medication held or discontinued during their entire hospitalization. Also, the indication and continuation of home therapy was dependent upon reliable clinical notes and admission medical histories. Furthermore, no subgroup analysis was performed to identify risk characteristics for the safety and efficacy outcomes. Lastly, with the retrospective nature of this study, there was no follow-up assessment after hospital discharge, making it difficult to determine the true bleeding and thromboembolic complications.

As a result of this MUE, health system changes were implemented to improve the safe and effective use of these oral anticoagulants. The orderset for both of these anticoagulants was updated to reinforce the FDA approved indications and dosing, along with manufacturer recommended transitions between anticoagulants. To increase patient education, an alert was built to notify pharmacists to educate patients on these new oral anticoagulants prior to discharge. Continued evaluation of patients on these oral anticoagulants will determine the final impact of this MUE on the health-system.

Conclusion

This medication utilization evaluation within a large, multi-center health system focused on the utilization of dabigatran and rivaroxaban therapy. Anticoagulant therapy was appropriate for most encounters, utilizing FDA approved indications and dosing recommendations. In addition, rates of bleeding and thromboembolism were less than or similar compared to clinical trials. However, quality improvement efforts have been implemented to improve the appropriate and safe use of these anticoagulants. Overall, this medication utilization evaluation revealed the appropriate use of these new oral anticoagulants within this health system with few safety outcomes.

Table 1: Dosing and Transitions between Anticoagulants

	Dabigatran¹	Rivaroxaban²
Dosing Recommendations		
Non-valvular atrial fibrillation	<ul style="list-style-type: none"> • CrCl > 30 mL/min: 150 mg orally BID • CrCl 15-30 mL/min: 75 mg orally BID 	<ul style="list-style-type: none"> • CrCl > 50 mL/min: 20 mg orally daily • CrCl 30-50 mL/min: 15 mg orally daily
TKA/THA post-operative prophylaxis		<ul style="list-style-type: none"> • CrCl > 30 mL/min: 10 mg orally daily
DVT/PE Treatment		<ul style="list-style-type: none"> • CrCl > 50 mL/min: 15 mg orally BID for 3 weeks then 20 mg orally daily • CrCl 30-50: 15 mg orally BID for 3 weeks then 15 mg orally daily
Anticoagulation Transitioning		
Warfarin	<ul style="list-style-type: none"> • From warfarin, discontinue warfarin must be discontinued and initiate dabigatran started when INR < 2.0 • To warfarin: <ul style="list-style-type: none"> ○ CrCl > 50 mL/min: discontinue dabigatran 3 days after starting warfarin ○ CrCl of 31-50 mL/min: discontinue dabigatran 2 days after starting warfarin ○ CrCl of 15-30 mL/min: discontinue dabigatran 1 day after starting warfarin 	<ul style="list-style-type: none"> • From warfarin, discontinue warfarin and start rivaroxaban when INR < 3.0 • To warfarin, initiate warfarin 24 hours after discontinuing rivaroxaban and bridge with a parenteral anticoagulant until INR is therapeutic
UFH	<ul style="list-style-type: none"> • From UFH, initiate dabigatran at the time of UFH discontinuation • To UFH, discontinue dabigatran and initiate UFH based on estimated CrCl: <ul style="list-style-type: none"> ○ CrCl > 30 mL/min: wait 12 hours after last dose of dabigatran ○ CrCl 15-30 mL/min: wait 24 hours after last dose of dabigatran 	<ul style="list-style-type: none"> • From UFH, rivaroxaban therapy should be started once the UFH infusion has been stopped • To UFH, begin the continuous infusion UFH 24 hours after stopping the rivaroxaban
Other parenteral anticoagulants	<ul style="list-style-type: none"> • From another parenteral anticoagulant, start dabigatran within 2 hours of next scheduled dose of the discontinued agent • To another parenteral anticoagulant, discontinue dabigatran and initiate the anticoagulant based on estimated CrCl: <ul style="list-style-type: none"> ○ CrCl > 30 mL/min: wait 12 hours after last dose of dabigatran ○ CrCl 15-30 mL/min: wait 24 hours after last dose of dabigatran 	<ul style="list-style-type: none"> • From another parenteral anticoagulant, initiate rivaroxaban within 2 hours of the next scheduled dose of the discontinued agent • To another parenteral anticoagulant, begin the anticoagulant 24 hours after stopping rivaroxaban

CrCl = creatinine clearance; BID = twice daily; TKA = total knee arthroplasty;
THA = total hip arthroplasty; DVT = deep vein thrombosis; PE = pulmonary embolism;
INR = international normalized ratio; UFH = unfractionated heparin

Table 2: Baseline Characteristics

	Dabigatran Encounters (n=78)	Rivaroxaban Encounters (n=62)
Mean age – years (SD)	66.9 ± 13.7	62.8 ± 13.7
Male sex – n (%)	39 (50)	33 (53)
Weight, kg – median (IQR)	87 (72-99)	94 (77-103)
Creatinine Clearance – n (%)		
>50 mL/min	55 (70.5)	43 (69)
30-50 mL/min	16 (20.5)	16 (26)
< 30 mL/min	7 (9)	3 (5)

SD = standard deviation; IQR = interquartile range

Table 3: Indications for Use*

	Dabigatran Encounters (n=78) % (n)	Rivaroxaban Encounters (n=62) % (n)
FDA Approved Indications		
Non-valvular atrial fibrillation	93 (73)	37 (23)
Post-operative prophylaxis TKA	-	39 (24)
Post-operative prophylaxis THA	-	6 (4)
Non-FDA Approved Indications		
Prevention of recurrent VTE	7 (5)	-
Open reduction internal fixation prophylaxis	-	8 (5)
Peripheral vascular disease	-	3 (2)
DVT treatment	-	2 (1)
Paroxysmal supraventricular tachycardia	-	2 (1)
Genetic coagulopathies	-	2 (1)
Incision and drainage	-	2 (1)

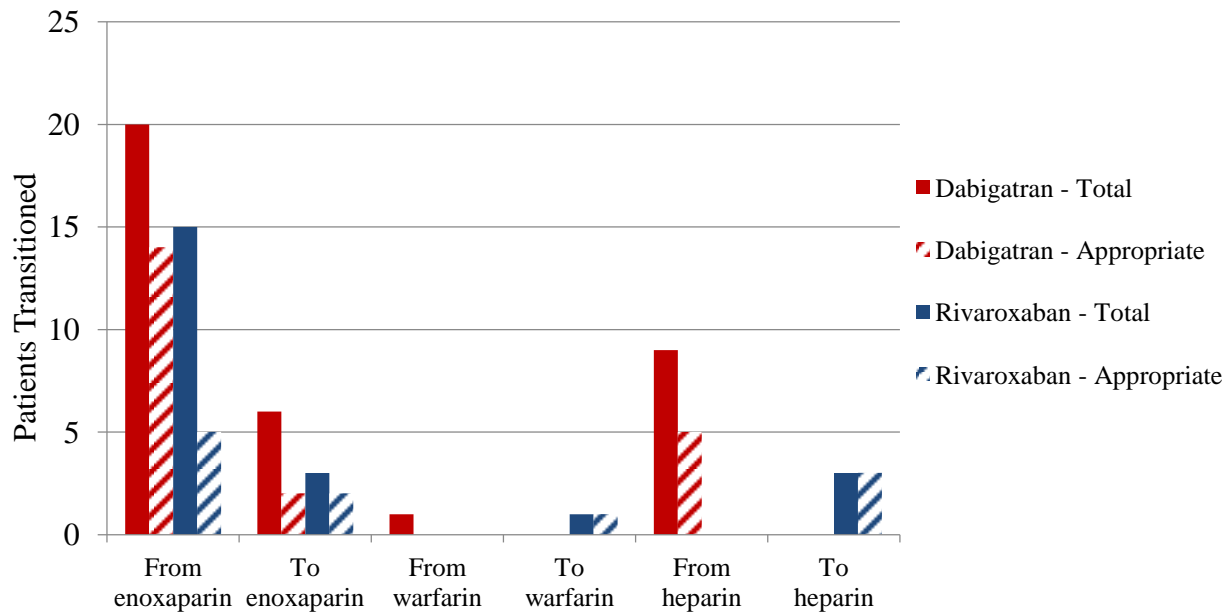
TKA = total knee arthroplasty; THA = total hip arthroplasty; VTE = venous thromboembolism; DVT = deep vein thrombosis

*FDA approved indications at the time of analysis (July 2012)

Table 4: Dose and Dosing Adjustments

	Dabigatran Encounters		Rivaroxaban Encounters	
Doses administered per patient				
Mean	6.4		3.2	
Median (IQR)	5 (3-7)		3 (2-4)	
Anticoagulant orders, % (n)	75 mg BID	83 (65)	10 mg daily	55 (34)
	150 mg BID	16 (12)	15 mg daily	21 (13)
	150 mg TID	1 (1)	20 mg daily	24 (15)
Doses administered, % (n)	75 mg	22 (107)	10 mg	110 (56)
	150 mg	78 (387)	15 mg	37 (19)
			20 mg	50 (25)
Appropriate dose, % (n)	87 (68)		92 (57)	
Appropriate renal dose adjustment, % (n)	55 (6)		79 (15)	

Figure 1: Transitioning Between Anticoagulant Therapy



References

1. Pradaxa@[package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2012.
2. Xarelto@[package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2012.
3. FDA expands use of Xarelto to treat, reduce recurrence of blood clots. Food and Drug Administration Website. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm326654.htm>. Nov 2012. Accessed May 6, 2013.
4. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361(12):1139-51.
5. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365:883-91.
6. Eriksson BI, Borris LC, Friedman RJ, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med*. 2008;358:2765-75.
7. Kakkar AK, Brenner B, Dahl O, et al. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet*. 2008;372:31-9.
8. Lassen MR, Agen W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after knee arthroplasty. *N Engl J Med*. 2008;358:2776-86.
9. Turpie AG, Lassen MR, Davidson BL, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *Lancet*. 2009;373:1673-80.
10. Bauersachs R, Berkowitz S, Brenner B, et al. Oral rivaroxaban for symptomatic venous thromboembolism. *NEJM*. 2010;363(26):2499-510.
11. Bauersachs R, Berkowitz S, Brenner B, et al. Oral rivaroxaban for symptomatic pulmonary embolism. *NEJM*. 2012;5;366(14):1287-97.
12. FDA drug safety communication: safety review of post-market reports of serious bleeding events with anticoagulant Pradaxa. Food and Drug Administration Website. www.fda.gov/Drugs/DrugSafety/ucm282724.htm#data. Dec 2011. Accessed May 6, 2013.
13. Drug report: Xarelto. Adverse Events Website. <http://www.adverseevents.com/drugdetail.php?AEDrugID=5158&BrandName=XARELTO&AEMode=HLT>. Aug 2012. Accessed May 6, 2013.
14. National patient safety goals NPSG 03.05.01. The Joint Commission Website. www.jointcommission.org/assets/1/18/NPSG_Chapter_Jan2013_HAP.pdf. Jan 2013. Accessed May 6, 2013.
15. Nutescu E, Wittkowsky A, Burnett A, Merli G, Ansell J, Garcia D. Delivery of optimized inpatient anticoagulation therapy: consensus statement from the Anticoagulation Forum. *Ann Pharmacother*. 2013;47:714-24.