CHAPTER **42**

XARELTO (RIVAROXABAN), FOR DEEP VEIN THROMBOSIS PROPHYLAXIS IN FOOT AND ANKLE SURGERY: An Introduction

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INTRODUCTION

Xarelto (rivaroxaban, Janssen Pharmaceuticals) is a new oral anticoagulation agent approved and indicated for deep venous thrombosis (DVT) prophylaxis in orthopedic major joint replacement surgery. The convenience and safety of this medication over other traditional anticoagulants make it especially appealing for foot and ankle surgical patients. Foot and ankle surgery patients, soon after the operation, may find it painful and difficult to report for venipuncture and laboratory testing necessary with traditional anticoagulation dosing in addition to visiting the surgeon for needed postoperative assessments and dressing changes. Short-term injectable anticoagulation bridging agents may be needed as well, until more traditional anticoagulation medications become effective after an initial latency period, and are costly. A medication that would obviate these short comings, but still be effective would be welcomed. This monograph is intended to provide an introduction to Xarelto and its use in DVT prophylaxis. The senior author has found patient acceptance and outcomes good in a limited number of patients.

PACKAGE INSERT HIGHLIGHTS: REVISED EDITION 08/2013

Xarelto is an orally available factor Xa inhibitor that selectively blocks the active site of factor Xa and does not require a cofactor. Black box warnings include primarily risks for chronic users who discontinue dosing prematurely resulting in premature thromboembolic events and spinal/epidural hematoma in patients undergoing spinal puncture or neuraxial anesthesia. The 15 mg and 20 mg tablets should be taken with food, while the 10 mg tablet can be taken with or without food. Contraindications are patients with active pathological bleeding or severe hypersensitivity to the drug. Drug interactions are with medications that are combined P-gp and Cytochrome P450 3A4 inhibitors such as ketoconazole, ritonavir, clarithromycin, erythromycin, and fluconazole that could prolong PT and result in increased bleeding. Also, avoid concomitant use with P-gp and Cytochrome P450 3A4 inducers such as St. John's Wort, carbamazepine, phenytoin, and rifampin that may reduce efficacy. It is not used in patients with artificial heart valves. Dosage for prophylaxis of DVT following hip or knee replacement surgery is 10 mg orally once daily with or without food dosed at about the same time each day. The most common adverse reaction was bleeding, >5%.

In use as prophylaxis for DVT following orthopedic surgery, Xarelto is recommended to be initiated orally 10 mg with or without food, at least 6 to 10 hours after surgery once hemostasis has been established. For patients after hip replacement surgery, treatment duration recommendation is 35 days. Treatment duration recommendation after knee replacement surgery is 12 days. (Author's Note: No recommendations are noted for any other orthopedic or podiatric procedures in the package insert, with or without immobilization.) If ongoing anticoagulation with Xarelto needs to be discontinued to reduce the risk of bleeding with surgical or other procedures, the Xarelto should be stopped at least 24 hours before the procedure. The medication is recommended to be taken about the same time every day, and as close as possible to the time typically dosed if a dose is missed.

LITERATURE REVIEW

In 2011, Patel et al reviewed information on the efficacy and safety of the medication. They found in patients with atrial fibrillation, rivaroxaban was noninferior to warfarin for the prevention of stroke or systemic embolism. In their literature review section they referenced with supporting literature statements such as: rivaroxaban may provide more consistent and predictable anticoagulation than warfarin as well as it prevented venous thromboembolism more effectively than Lovenox (enoxaparin, Sanofi) in pateints undergoing orthopedic surgery. They further stated within

their literature review on venous thrombosis prophylaxis that rivaroxaban was noninferior to enoxaparin (Lovenox) followed by warfarin in a study involving patients with established venous thrombosis by Einstein in 2010. The Patel et al article further noted in terms of complications with rivaroxaban use: no significant difference with warfarin with respect to rates of major or nonmajor clinically relevant bleeding. Bleeding that proved fatal or involved a critical anatomic site occurred less frequently in the rivaroxaban group, mainly because of lower rates of hemorrhagic stroke and other intracranial bleeding. In contrast, bleeding from gastrointestinal sites, including upper, lower, and rectal sites, occurred more frequently in the rivaroxaban group, as did bleeding that led to a drop in hemoglobin level or bleeding that required transfusion.

In a 2013 article by Baron et al, the authors reviewed current studies and trends for the perioperative management of patients taking anticoagulation medications including rivaroxaban. Important points on the reversibility of the medication were reviewed. The authors referenced a 2012 research paper by Dzik in their article, which noted the reliable reversibility of the effects of the newer anticoagulation agents (such as rivaroxaban a direct factor Xa inhibitor), has not been proved. The effects of rivaroxaban were reversed in 12 healthy volunteers after the administration of 4-factor prothrombin complex concentrates as described by Eerenberg et al in a 2011 article. Baron et al noted rivaroxaban is not dialyzable. Additionally, Baron et al recommend delaying restarting rivaroxaban for 48 hours after high-risk procedures because the full anticoagulatory effect occurs shortly after administration and there are no reversal agents for this medication.

CONCLUSION

Xarelto seems to be a promising new oral anticoagulation agent in the management of DVT prophylaxis following orthopedic surgery. No specific podiatric surgery studies are available, only hip and knee replacement surgery applications. No data or recommendations are available for duration of use after foot and ankle surgery. The senior author has continued dosing the medication as warfarin is dosed, until immobilization was discontinued and there was return to active independent weight-bearing activity, but experience is only in a limited number of patients. The quick onset obviates the need for initial bridging injectable medications early after surgery. The lack of need for regular venipuncture and laboratory testing is convenient for the relatively immobile early postoperative foot and ankle surgical patient. In 2011, Prescriber's Letter reported Xeralto costs approximately $260.00 per month and Warfarin $80.00 per month with INR monitoring only once a month (not including the cost of injectable initial bridging agents.) Hopefully this monograph helps introduce this medication for consideration and further review in podiatric patients in consultation with internal medicine. Monitoring the literature for more reports and further studies are needed on Xarelto use, especially for foot and ankle surgery applications. *This report is not an endorsement of the medication and the authors have received no financial incentives in preparing this paper.*

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