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## **XARELTO<sup>®</sup> (rivaroxaban) for Reducing the Risk of Stroke and Systemic Embolism in Patients With Nonvalvular Atrial Fibrillation (AF) and for the Treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)**

**OUR GUEST SPEAKER WILL BE**

**Frank Rasler, MD, MPH**

*President, Atlanta HealthCare Associates*

*Atlanta, GA*

Dr. Rasler is a paid speaker for Janssen Pharmaceuticals, Inc.

**Tuesday, December 08, 2015 at 12:30 PM**

**The Ritz-Carlton Lodge, Reynolds Plantation**

Sassafras Room, 1 Lake Oconee Trail, Greensboro, GA 30642 Phone: (706) 467-0600

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### **INDICATIONS**

XARELTO<sup>®</sup> is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AF).

There are limited data on the relative effectiveness of XARELTO<sup>®</sup> and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well controlled.

XARELTO<sup>®</sup> is indicated for the treatment of deep vein thrombosis (DVT). XARELTO<sup>®</sup> is indicated for the treatment of pulmonary embolism (PE). XARELTO<sup>®</sup> is indicated for the reduction in the risk of recurrence of DVT and of PE following initial 6 months treatment for DVT and/or PE.

**Please see additional Important Safety Information, including Boxed WARNINGS, on next page.**

**Please see accompanying full Prescribing Information, including Boxed WARNINGS, or visit [www.XARELTOhcp.com](http://www.XARELTOhcp.com).**

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## IMPORTANT SAFETY INFORMATION

### WARNING: (A) PREMATURE DISCONTINUATION OF XARELTO® INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

#### A. PREMATURE DISCONTINUATION OF XARELTO® INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including XARELTO®, increases the risk of thrombotic events. If anticoagulation with XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

#### B. SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas have occurred in patients treated with XARELTO® who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- ◆ Use of indwelling epidural catheters
- ◆ Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants, *see Drug Interactions*
- ◆ A history of traumatic or repeated epidural or spinal punctures
- ◆ A history of spinal deformity or spinal surgery
- ◆ Optimal timing between the administration of XARELTO® and neuraxial procedures is not known

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

## CONTRAINDICATIONS

- ◆ Active pathological bleeding
- ◆ Severe hypersensitivity reaction to XARELTO® (eg, anaphylactic reactions)

## WARNINGS AND PRECAUTIONS

- ◆ **Increased Risk of Thrombotic Events After Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including XARELTO®, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from XARELTO® to warfarin in clinical trials in atrial fibrillation patients. If XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- ◆ **Risk of Bleeding:** XARELTO® increases the risk of bleeding and can cause serious or fatal bleeding. Promptly evaluate any signs or symptoms of blood loss and consider the need for blood replacement. Discontinue XARELTO® in patients with active pathological hemorrhage.
  - A specific antidote for rivaroxaban is not available. Because of high plasma protein binding, rivaroxaban is not expected to be dialyzable.
  - Concomitant use of other drugs affecting hemostasis increases the risk of bleeding. These include aspirin, P2Y<sub>12</sub> platelet inhibitors, other antithrombotic agents, fibrinolytic therapy, and NSAIDs.
- ◆ **Spinal/Epidural Anesthesia or Puncture:** When neuraxial anesthesia (spinal/epidural anesthesia) or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis. To reduce the potential risk of bleeding associated with the concurrent use of rivaroxaban and epidural or spinal anesthesia/analgesia or spinal puncture, consider the pharmacokinetic profile of rivaroxaban. Placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of rivaroxaban is low; however, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known. An epidural catheter should not be removed earlier than 18 hours after the last administration of XARELTO®. The next XARELTO® dose is not to be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, the administration of XARELTO® is to be delayed for 24 hours. Should the physician decide to administer anticoagulation in the context of epidural or spinal anesthesia/analgesia or lumbar puncture, monitor frequently to detect any signs or symptoms of neurological impairment, such as midline back pain, sensory and motor deficits (numbness, tingling, or weakness in lower limbs), or bowel and/or bladder dysfunction. Instruct patients to immediately report if they experience any of the above signs or symptoms. If signs or

symptoms of spinal hematoma are suspected, initiate urgent diagnosis and treatment including consideration for spinal cord decompression even though such treatment may not prevent or reverse neurological sequelae.

## ◆ Use in Patients With Renal Impairment:

- **Nonvalvular Atrial Fibrillation:** Avoid the use of XARELTO® in patients with creatinine clearance (CrCl) <15 mL/min, since drug exposure is increased. Discontinue XARELTO® in patients who develop acute renal failure while on XARELTO®.
- **Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and Reduction in the Risk of Recurrence of DVT and of PE:** Avoid the use of XARELTO® in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population.
- **Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery:** Avoid the use of XARELTO® in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population. Observe closely and promptly evaluate any signs or symptoms of blood loss in patients with CrCl 30 to 50 mL/min. Patients who develop acute renal failure while on XARELTO® should discontinue the treatment.

◆ **Use in Patients With Hepatic Impairment:** No clinical data are available for patients with severe hepatic impairment. Avoid use of XARELTO® in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy, since drug exposure and bleeding risk may be increased.

◆ **Use With P-gp and Strong CYP3A4 Inhibitors or Inducers:** Avoid concomitant use of XARELTO® with combined P-gp and strong CYP3A4 inhibitors (eg, ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir/ritonavir, and conivaptan). Avoid concomitant use of XARELTO® with drugs that are P-gp and strong CYP3A4 inducers (eg, carbamazepine, phenytoin, rifampin, St. John's wort).

◆ **Risk of Pregnancy-Related Hemorrhage:** In pregnant women, XARELTO® should be used only if the potential benefit justifies the potential risk to the mother and fetus. XARELTO® dosing in pregnancy has not been studied. The anticoagulant effect of XARELTO® cannot be monitored with standard laboratory testing and is not readily reversed. Promptly evaluate any signs or symptoms suggesting blood loss (eg, a drop in hemoglobin and/or hematocrit, hypotension, or fetal distress).

◆ **Patients With Prosthetic Heart Valves:** The safety and efficacy of XARELTO® have not been studied in patients with prosthetic heart valves. Therefore, use of XARELTO® is not recommended in these patients.

◆ **Acute PE in Hemodynamically Unstable Patients/Patients Who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of XARELTO® is not recommended acutely as an alternative to unfractionated heparin in patients with pulmonary embolism who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

## DRUG INTERACTIONS

- ◆ Avoid concomitant use of XARELTO® with other anticoagulants due to increased bleeding risk, unless benefit outweighs risk. Promptly evaluate any signs or symptoms of blood loss if patients are treated concomitantly with aspirin, other platelet aggregation inhibitors, or NSAIDs.
- ◆ XARELTO® should not be used in patients with CrCl 15 to 80 mL/min who are receiving concomitant combined P-gp and moderate CYP3A4 inhibitors unless the potential benefit justifies the potential risk.

## USE IN SPECIFIC POPULATIONS

- ◆ **Pregnancy Category C:** XARELTO® should be used during pregnancy only if the potential benefit justifies the potential risk to mother and fetus. There are no adequate or well-controlled studies of XARELTO® in pregnant women, and dosing for pregnant women has not been established. Use XARELTO® with caution in pregnant patients because of the potential for pregnancy-related hemorrhage and/or emergent delivery with an anticoagulant that is not readily reversible. The anticoagulant effect of XARELTO® cannot be reliably monitored with standard laboratory testing.
- ◆ **Labor and Delivery:** Safety and effectiveness of XARELTO® during labor and delivery have not been studied in clinical trials.
- ◆ **Nursing Mothers:** It is not known if rivaroxaban is excreted in human milk.
- ◆ **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established.
- ◆ **Females of Reproductive Potential:** Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician.

## OVERDOSAGE

- ◆ Discontinue XARELTO® and initiate appropriate therapy if bleeding complications associated with overdosage occur. A specific antidote for rivaroxaban is not available. The use of activated charcoal to reduce absorption in case of XARELTO® overdose may be considered. Due to the high plasma protein binding, rivaroxaban is not expected to be dialyzable.

## ADVERSE REACTIONS IN CLINICAL STUDIES

- ◆ The most common adverse reactions with XARELTO® were bleeding complications.

**Please see accompanying full Prescribing Information, including Boxed WARNINGS; or visit [www.XARELTOhcp.com](http://www.XARELTOhcp.com).**