HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use XARELTO® (rivaroxaban) safely and effectively. See full prescribing information for XARELTO.

XARELTO (rivaroxaban) tablets, for oral use
Initial U.S. Approval: 2011

WARNING: (A) PREMATURE DISCONTINUATION OF XARELTO INCREASES THE RISK OF THROMBOTIC EVENTS, and (B) SPINAL/EPIDURAL HEMATOMA
See full prescribing information for complete boxed warning

PREMATURE DISCONTINUATION OF XARELTO INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including XARELTO, increases the risk of thrombotic events. To reduce this risk, consider coverage with another anticoagulant if XARELTO is discontinued for a reason other than pathological bleeding or completion of a course of therapy (2.2, 2.6, 5.1, 14.1).

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 (5.2, 5.3, 6.2).

Monitor patients frequently for signs and symptoms of neurological impairment and if observed, treat urgently. Consider the benefits and risks before neuraxial intervention in patients who are or who need to be anticoagulated (5.3).

----------RECENT MAJOR CHANGES----------

Boxed Warning	08/2013
Dosage and Administration (2.8)	03/2013
Dosage and Administration (2.5)	01/2014
Warnings and Precautions (5.1, 5.8)	08/2013
Warnings and Precautions (5.2, 5.6, 5.8, 5.9)	01/2014

----------INDICATIONS AND USAGE----------

XARELTO is a factor Xa inhibitor indicated:

- to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (1.1)
- for the treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), and for the reduction in the risk of recurrence of DVT and of PE (1.2, 1.3, 1.4)
- for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery (1.5)

----------DOSAGE AND ADMINISTRATION----------

- Take 15 mg and 20 mg tablets with food; take 10 mg tablets with or without food (2.1)
- Nonvalvular Atrial Fibrillation:
  - For patients with CrCl >50 mL/min: 20 mg orally, once daily **with the evening meal** (2.3)
  - For patients with CrCl 15 - 50 mL/min: 15 mg orally, once daily **with the evening meal** (2.3)
- Treatment of DVT, PE, and Reduction in the Risk of Recurrence of DVT and of PE: 15 mg orally twice daily with food for the first 21 days for the initial treatment of acute DVT or PE. After the initial treatment period, 20 mg orally once daily with food for the remaining treatment and the long-term reduction in the risk of recurrence of DVT and of PE. (2.4)
- Prophylaxis of DVT Following Hip or Knee Replacement Surgery: 10 mg orally, once daily with or without food (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 10 mg, 15 mg, and 20 mg (3)

----------CONTRAINDICATIONS----------

- Active pathological bleeding (4)
- Severe hypersensitivity reaction to XARELTO (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk of bleeding: XARELTO can cause serious and fatal bleeding. Promptly evaluate signs and symptoms of blood loss. (5.2)
- Pregnancy-related hemorrhage: Use XARELTO with caution in pregnant women due to the potential for obstetric hemorrhage and/or emergent delivery. Promptly evaluate signs and symptoms of blood loss. (5.7)
- Prosthetic heart valves: XARELTO use not recommended (5.8)

----------ADVERSE REACTIONS----------

The most common adverse reaction (>5%) was bleeding. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Pharmaceuticals, Inc. at 1-800-526-7736 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------

- Combined P-gp and strong CYP3A4 inhibitors and inducers: Avoid concomitant use (7.1, 7.2)
- Anticoagulants: Avoid concomitant use (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Nursing mothers: discontinue drug or discontinue nursing (8.3)
- Renal impairment: Avoid or adjust dose based on CrCl (8.7)
- Hepatic impairment: Avoid use in patients with Child-Pugh B and C hepatic impairment or with any degree of hepatic disease associated with coagulopathy (8.8)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 02/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING 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 *[see Dosage and Administration (2.2, 2.6), Warnings and Precautions (5.1), and Clinical Studies (14.1)]*.

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**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**

***[see Warnings and Precautions (5.2, 5.3) and Adverse Reactions (6.2)]*.**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary *[see Warnings and Precautions (5.3)]*.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis *[see Warnings and Precautions (5.3)]*.

1 INDICATIONS AND USAGE

1.1 Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation

XARELTO is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

There are limited data on the relative effectiveness of XARELTO and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well-controlled *[see Clinical Studies (14.1)]*.

1.2 Treatment of Deep Vein Thrombosis

XARELTO is indicated for the treatment of deep vein thrombosis (DVT).

1.3 Treatment of Pulmonary Embolism

XARELTO is indicated for the treatment of pulmonary embolism (PE).

1.4 Reduction in the Risk of Recurrence of Deep Vein Thrombosis and of Pulmonary Embolism

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

1.5 Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery

XARELTO is indicated for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery.

2 DOSAGE AND ADMINISTRATION

Indication	Dosage	
Reduction in Risk of Stroke in Nonvalvular Atrial Fibrillation (2.3)	CrCl >50 mL/min:	20 mg once daily **with the evening meal**
	CrCl 15 to 50 mL/min:	15 mg once daily **with the evening meal**
Treatment of DVT (2.4) **Treatment of PE (2.4)**	15 mg twice daily with food, for first 21 days **▼after 21 days, transition to ▼** 20 mg once daily with food, for remaining treatment	
Reduction in the Risk of Recurrence of DVT and of PE (2.4)	20 mg once daily with food	
Prophylaxis of DVT Following Hip or Knee Replacement Surgery (2.5)	Hip replacement:	10 mg once daily for 35 days
	Knee replacement:	10 mg once daily for 12 days

2.1 Important Food Effect Information

The 15 mg and 20 mg XARELTO tablets should be taken with food, while the 10 mg tablet can be taken with or without food *[see Clinical Pharmacology (12.3)]*.

In the nonvalvular atrial fibrillation efficacy study XARELTO was taken with the evening meal.

2.2 Switching to and from XARELTO

Switching from Warfarin to XARELTO - When switching patients from warfarin to XARELTO, discontinue warfarin and start XARELTO as soon as the International Normalized Ratio (INR) is below 3.0 to avoid periods of inadequate anticoagulation.

Switching from XARELTO to Warfarin - No clinical trial data are available to guide converting patients from XARELTO to warfarin. XARELTO affects INR, so INR measurements made during coadministration with warfarin may not be useful for determining the appropriate dose of warfarin. One approach is to discontinue XARELTO and begin both a parenteral anticoagulant and warfarin at the time the next dose of XARELTO would have been taken.

Switching from XARELTO to Anticoagulants other than Warfarin - For patients currently taking XARELTO and transitioning to an anticoagulant with rapid onset, discontinue XARELTO and give the first dose of the other anticoagulant (oral or parenteral) at the time that the next XARELTO dose would have been taken *[see Drug Interactions (7.3)]*.

Switching from Anticoagulants other than Warfarin to XARELTO - For patients currently receiving an anticoagulant other than warfarin, start XARELTO 0 to 2 hours prior to the next scheduled evening administration of the drug (e.g., low molecular weight heparin or non-warfarin oral anticoagulant) and omit administration of the other anticoagulant. For unfractionated heparin being administered by continuous infusion, stop the infusion and start XARELTO at the same time.

2.3 Nonvalvular Atrial Fibrillation

For patients with creatinine clearance (CrCl) >50 mL/min, the recommended dose of XARELTO is 20 mg taken orally once daily with the evening meal. For patients with CrCl 15 to 50 mL/min, the recommended dose is 15 mg once daily with the evening meal *[see Use in Specific Populations (8.7)]*.

2.4 Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and Reduction in the Risk of Recurrence of DVT and of PE

The recommended dose of XARELTO for the initial treatment of acute DVT and/or PE is 15 mg taken orally twice daily with food for the first 21 days. After this initial treatment period, the recommended dose of XARELTO is 20 mg taken orally once daily with food, at approximately the same time each day. The recommended dose of XARELTO for reduction in the risk of recurrence of DVT or PE is 20 mg taken orally once daily with food at approximately the same time each day *[see Clinical Studies (14.2)]*.

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