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Coverage Policy Number **IP0032**

Rivaroxaban

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Related Coverage Resources

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Overview

This policy supports medical necessity review for rivaroxaban tablets and oral suspension (**Xarelto**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Rivaroxaban (Xarelto) is considered medically necessary when there is documentation of ONE of the following:

1. **Atrial Fibrillation (or Atrial Flutter).**

2. **Coronary Artery Disease.** Individual meets the following criteria:
   Concomitant use of aspirin at least 75 mg daily

3. **Deep Vein Thrombosis in Individuals Undergoing Knee or Hip Replacement Surgery, Prophylaxis.**

4. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Individual meets **ONE** of the following:
   A) Xarelto tablets are requested
   B) If Xarelto oral suspension is being requested, documented inability to swallow or achieve the desired dose with Xarelto tablets

5. **Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence.**

6. **Peripheral Artery Disease.** Individual meets the following criteria:
   Concomitant use of aspirin at least 75 mg daily

7. **Thromboprophylaxis in an individual with Congenital Heart Disease.** Individual meets **BOTH** of the following criteria:
   A) Undergone the Fontan procedure
   B) If Xarelto oral suspension is being requested, documented inability to swallow or achieve the desired dose with Xarelto tablets

8. **Venous Thromboembolism in Acutely Ill Individuals, Prophylaxis.**
   This includes post-discharge thromboprophylaxis for an individual hospitalized with coronavirus disease 19 (COVID-19).

9. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Individual meets **BOTH** of the following criteria:
   Examples of other thromboembolic-related conditions include superficial vein thrombosis, splanchnic vein thrombosis, hepatic vein thrombosis, prophylaxis of venous thromboembolism in high-risk individuals.
   A) Documentation of **ONE** of the following:
      i. Failure, contraindication, or inadequate response to **ONE** of the following: warfarin, fondaparinux injection, or a low molecular weight heparin product.
      ii. Previously started on Xarelto for the treatment of an acute thromboembolic condition.

   B) If Xarelto oral suspension is being requested, documented inability to swallow or achieve the desired dose with Xarelto tablets

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of Rivaroxaban (Xarelto) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial responses.

Authorization Duration

Initial approval duration:
- Atrial Fibrillation (or Atrial Flutter): up to 12 months
- Deep Vein Thrombosis in Individuals Undergoing Knee or Hip Replacement Surgery, Prophylaxis: up to 60 days
- Deep Vein Thrombosis or Pulmonary Embolism, Treatment: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence: up to 12 months
- Coronary Artery Disease: up to 12 months
- Peripheral Artery Disease: up to 12 months

- Prophylaxis of Venous Thromboembolism in Acutely Ill Individuals: up to 60 days
- Thromboprophylaxis in a Patient with Congenital Heart Disease: up to 12 months
- Treatment or Prevention of Other Thromboembolic-Related Conditions: up to 6 months

Reauthorization approval duration:

- Atrial Fibrillation (or Atrial Flutter): up to 12 months
- Deep Vein Thrombosis in Individuals Undergoing Hip or Knee Replacement Surgery, Prophylaxis: Not applicable
- Deep Vein Thrombosis or Pulmonary Embolism, Treatment: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence: up to 12 months
- Coronary Artery Disease: up to 12 months
- Peripheral Artery Disease: up to 12 months
- Prophylaxis of Venous Thromboembolism in Acutely Ill Individuals: up to 60 days
- Thromboprophylaxis in a Patient with Congenital Heart Disease: up to 12 months
- Treatment or Prevention of Other Thromboembolic-Related Conditions: up to 6 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven including the following (this list may not be all inclusive):

Prophylaxis of Venous Thromboembolism in Individuals with Factor V Leiden thrombophilia and Antiphospholipid syndrome. There is limited evidence to the support the use of direct-acting oral anticoagulants (DOACs), including Eliquis for Factor V Leiden Thrombophilia. Eliquis and other DOACs are not recommended for use in individuals with triple-positive antiphospholipid syndrome (APS).[1] For individuals with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2 glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.[1]

Background

Overview

Xarelto, an oral Factor Xa inhibitor, is indicated for the following uses:[1]

- **Atrial fibrillation**, non-valvular, to reduce the risk of stroke and systemic embolism in adults.
- **Coronary artery disease**, in combination with aspirin, to reduce the risk of major adverse cardiovascular events in adults.
- **Prophylaxis of deep vein thrombosis (DVT),** which may lead to pulmonary embolism (PE), in patients undergoing knee or hip replacement surgery in adults.
- **Prophylaxis of venous thromboembolism in acutely ill medical patients**, in adults at risk for thromboembolic complications not at high risk of bleeding.
- **Peripheral artery disease**, in adults, including patients after recent lower extremity revascularization due to symptomatic peripheral artery disease, in combination with aspirin to reduce the risk of major thrombotic vascular events.
- **Treatment of DVT** and **PE**, as well as **reduction in the risk of recurrence of DVT and/or PE** in patients at continued risk for recurrent DVT and/or PE after completion of initial treatment. These indications includes patients birth to < 18 years of age as well as adults.
- **Thromboprophylaxis in a patient with congenital heart disease after the Fontan procedure**, in pediatric patients ≥ 2 years of age.

Guidelines

Guidelines are available which support the use of direct oral anticoagulants (DOACs) in their commonly used clinical settings, such as DVT/PE[2-5] and atrial fibrillation[6,7]. In patients who are eligible for a DOAC, these are generally preferred over vitamin K antagonists (e.g., warfarin). It is noted that in the randomized trials in atrial

fibrillation, DOACs were consistently at least non-inferior to warfarin regarding the composite of stroke or systemic embolism and were associated with lower risk of serious bleeding.[7]

Anticoagulants and Coronavirus Disease 19 (COVID-19)
Several clinical practice guidelines have been published with regard to use of anticoagulant therapy in the management of COVID-19. Per National Institutes of Health treatment guidelines regarding antithrombotic therapy in patients with COVID-19 (updated October 27, 2021), hospitalized patients with COVID-19 should not be routinely discharged from the hospital while on venous thromboembolism (VTE) prophylaxis.[8] For patients at low risk for bleeding and high risk for VTE, continuing anticoagulation with an FDA-approved regimen for extended VTE prophylaxis may be considered, as per protocols for patients without COVID-19. Of note, Xarelto is FDA-approved for prophylaxis of VTE in acutely ill medical patients. Other guidelines have similar recommendations.[9-11]

Other Uses with Supportive Evidence
Although data are not robust regarding use of DOACs in off-label thromboembolic-related conditions, CHEST guidelines (2012) suggest anticoagulation for certain patients with superficial vein thrombosis, symptomatic splanchnic thromboses (portal, mesenteric, and/or splenic vein), or symptomatic hepatic vein thrombosis.[2] The guidelines acknowledge the limited available data in these settings, and all are given Grade 2C recommendations (weak recommendation, low-quality evidence). The 2016 CHEST guideline update did not address these conditions or comment on the role of DOACs.[3] The choice of anticoagulant is often individualized based on patient-specific factors; therefore, for certain patients, DOAC use may be considered in practice. Evidence for DOACs is limited for off-label scenarios; in general, agents such as vitamin K antagonists (e.g., warfarin) and low molecular weight heparin have more clinical experience in these settings.

Dosing and Administration[1]

Recommended Dosage in Adults

Indication	Renal Considerations	Dosage	Food/Timing
Reduction in Risk of Stroke in Nonvalvular Atrial Fibrillation	CrCl >50 mL/min	20 mg once daily	Take with evening meal
	CrCl ≤50 mL/min	15 mg once daily	Take with evening meal
Treatment of DVT and/or PE	CrCl ≥15 mL/min	15 mg twice daily **▼ after 21 days, transition to ▼** 20 mg once daily	Take with food, at the same time each day
	CrCl <15 mL/min	Avoid use	Avoid use
Reduction in the Risk of Recurrence of DVT and/or PE in patients at continued risk for DVT and/or PE	CrCl ≥15 mL/min	10 mg once daily, after at least 6 months of standard anticoagulant treatment	Take with or without food
	CrCl <15 mL/min	Avoid use	Avoid use
Prophylaxis of DVT Following:			
Hip Replacement Surgery	CrCl ≥15 mL/min	10 mg once daily for 35 days, 6-10 hours after surgery once hemostasis has been established	Take with or without food
	CrCl <15 mL/min	Avoid use	Avoid use
Knee Replacement Surgery	CrCl ≥15 mL/min	10 mg once daily for 12 days, 6-10 hours after surgery once hemostasis has been established	Take with or without food
	CrCl <15 mL/min	Avoid use	Avoid use

Prophylaxis of VTE in Acutely Ill Medical Patients at Risk for Thromboembolic Complications Not at High Risk of Bleeding	CrCl ≥15 mL/min	10 mg once daily, in hospital and after hospital discharge, for a total recommended duration of 31 to 39 days	Take with or without food
	CrCl <15 mL/min	Avoid use	Avoid use
Reduction of Risk of Major Cardiovascular Events (CV Death, MI, and Stroke) in CAD	No dose adjustment needed based on CrCl	2.5 mg twice daily, plus aspirin (75-100 mg) once daily	Take with or without food
Reduction of Risk of Major Thrombotic Vascular Events in PAD, Including Patients after Lower Extremity Revascularization due to Symptomatic PAD	No dose adjustment needed based on CrCl	2.5 mg twice daily, plus aspirin (75-100 mg) once daily. When starting therapy after a successful lower extremity revascularization procedure, initiate once hemostasis has been established.	Take with or without food

Recommended Dosage in Pediatric Patients

Recommended Dosage in Pediatric Patients Birth to Less than 18 Years for Treatment of and Reduction in Risk of Recurrent VTE

Dosage Form	Body Weight	Dosage			Total Daily Dose
		Once a Day	2 Times a Day	3 Times a Day	
Oral Suspension Only	2.6 kg to 2.9 kg			0.8 mg	2.4 mg
	3 kg to 3.9 kg			0.9 mg	2.7 mg
	4 kg to 4.9 kg			1.4 mg	4.2 mg
	5 kg to 6.9 kg			1.6 mg	4.8 mg
	7 kg to 7.9 kg			1.8 mg	5.4 mg
	8 kg to 8.9 kg			2.4 mg	7.2 mg
	9 kg to 9.9 kg			2.8 mg	8.4 mg
	10 kg to 11.9 kg			3 mg	9 mg
	12 kg to 29.9 kg		5 mg		10 mg
Oral Suspension or Tablets	30 kg to 49.9 kg	15 mg			15 mg
	≥50 kg	20 mg			20 mg

Recommended Dosage for Thromboprophylaxis in Pediatric Patients with Congenital Heart Disease

Dosage Form	Body Weight	Dosage		Total Daily Dose
		Once a Day	2 Times a Day	
Oral Suspension Only	7 kg to 7.9 kg		1.1 mg	2.2 ng
	8 kg to 9.9 kg		1.6 mg	3.2 ng

	10 kg to 11.9 kg		1.7 mg	3.4 mg
	12 kg to 19.9 kg		2 mg	4 mg
	20 kg to 29.9 kg		2.5 mg	5 mg
	30 kg to 49.9 kg	7.5 mg		7.5 mg
Oral Suspension or Tablets	≥50 kg	10 mg		10 mg

References

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