Drug Coverage Policy

Effective Date.....8/1/2024
Coverage Policy Number.....IP0032
Policy Title.....Xarelto

Anticoagulants – Xarelto

- Xarelto® (rivaroxaban tablets and oral suspension – Janssen)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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 include patients from 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.

Dosing and Administration

In the prescribing information for Xarelto tablets and oral suspension, it is noted that for adults who are unable to swallow whole tablets, Xarelto tablets (all strengths) may be crushed and mixed with applesauce immediately prior to use and administered orally.[1] Xarelto tablets (all strengths) may be crushed and suspended in water for administration via nasogastric or gastric tube. Xarelto oral suspension may also be given through nasogastric or gastric tube.

For pediatric patients, tablets must not be split in an attempt to provide a fraction of a tablet dose. For treatment of venous thromboembolism (VTE) and reduction in risk of VTE recurrence in pediatric patients, it is noted that oral suspension or tablets may be used for a patient weighing ≥ 30 kg; for patients weighing < 30 kg, oral suspension should be used. For thromboprophylaxis in pediatric patients with congenital heart disease after the Fontan procedure, oral suspension or tablets may be used for a patient weighing ≥ 50 kg; oral suspension is needed for a patient weighing < 50 kg. It is noted that there are no safety, efficacy, pharmacokinetic, and pharmacodynamic data to support the use of Xarelto 2.5 mg tablets in pediatric patients; therefore, Xarelto 2.5 mg tablets are not recommended in pediatric patients.

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] Guidelines from the Canadian Cardiovascular Society for peripheral arterial disease (2022) recommend Xarelto in combination with aspirin in selected patients with peripheral arterial disease (high risk of ischemic events).[8]

Anticoagulants and Coronavirus Disease 2019 (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 10, 2023), hospitalized patients with COVID-19 should not be routinely discharged from the hospital while on venous thromboembolism (VTE) prophylaxis.[9] For hospitalized patients, anticoagulant or antiplatelet therapy should not be used to prevent arterial thrombosis outside of the usual standard of care for patients without COVID-19. In nonhospitalized patients with COVID-19, it is not recommended to use anticoagulant and antiplatelet therapy for the prevention of VTE or arterial thrombosis, except in a clinical trial. Of note, Xarelto® (rivaroxaban tablets and oral suspension) is FDA-approved for prophylaxis of VTE in acutely ill medical patients; Eliquis is not indicated in this setting. Other guidelines have similar recommendations.[10-12]

Other Uses with Supportive Evidence

Although data are not robust regarding use of DOACs in other off-label thromboembolic-related conditions, American College of Chest Physicians (CHEST) guidelines (2021) suggest anticoagulation for certain patients (e.g., superficial vein thrombosis, antiphospholipid syndrome).[2] 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, there is more clinical experience with agents such as vitamin K antagonists (e.g., warfarin) and low molecular weight heparin in these settings.

Medical Necessity Criteria

Xarelto (tablets and oral suspension) are considered medically necessary when ONE of the following is met (1, 2, 3, 4, 5, 6, 7, 8, or 9):

FDA-Approved Indications

1. **Atrial Fibrillation (or Atrial Flutter).** Approve for 1 year if the patient meets both of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered.

2. **Coronary Artery Disease.** Approve for 1 year if the patient meets all of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient will be taking concomitant aspirin at least 75 mg daily; AND
   - **C)** If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered.

3. **Deep Vein Thrombosis in a Patient Undergoing Knee or Hip Replacement Surgery, Prophylaxis.** Approve for 60 days if the patient meets both of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered.

4. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Approve for 1 year if the patient meets one of the following (A or B):
   - **A)** Xarelto tablets: Approve.
   - **B)** Xarelto oral suspension: Approve if the patient meets one of the following (i or ii):
     - **i.** Patient is unable to have Xarelto tablets appropriately administered; OR
     - **ii.** The prescribed Xarelto dose cannot be achieved by Xarelto 10 mg, 15 mg, or 20 mg tablets.

5. **Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence.** Approve for 1 year if the patient meets one of the following (A or B):
   - **A)** Xarelto tablets: Approve.
   - **B)** Xarelto oral suspension: Approve if the patient meets one of the following (i or ii):
     - **i.** Patient is unable to have Xarelto tablets appropriately administered; OR
     - **ii.** The prescribed Xarelto dose cannot be achieved by Xarelto 10 mg, 15 mg, or 20 mg tablets.

6. **Peripheral Artery Disease.** Approve for 1 year if the patient meets all of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient will be taking concomitant aspirin at least 75 mg daily; AND
   C) If Xarelto oral suspension is being requested, patient is unable to have Xarelto tablets appropriately administered.

7. **Thromboprophylaxis in a Patient with Congenital Heart Disease.** Approve for 1 year if the patient meets all of the following (A, B, and C):
   A) Patient is ≥ 2 years of age and < 18 years of age; AND
   B) Patient has undergone the Fontan procedure; AND
   C) If Xarelto oral suspension is being requested, patient meets one of the following (i or ii):
      i. Patient is unable to have Xarelto tablets appropriately administered; OR
      ii. The prescribed Xarelto dose cannot be achieved by Xarelto 10 mg, 15 mg, or 20 mg tablets.

8. **Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis.** Approve for 60 days if the patient meets both of the following (A and B):
   Note: This includes post-discharge thromboprophylaxis for a patient hospitalized with coronavirus disease 2019 (COVID-19).
   A) Patient is ≥ 18 years of age; AND
   B) If Xarelto oral suspension is being requested, patient is unable to have Xarelto tablets appropriately administered.

Other Uses with Supportive Evidence

9. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Approve for 6 months if the patient meets both of the following (A and B):
   Note: Examples of other thromboembolic-related conditions include superficial vein thrombosis, splanchnic vein thrombosis, hepatic vein thrombosis, or prophylaxis of venous thromboembolism in a high-risk patient.
   A) Patient meets one of the following (i or ii):
      i. Patient has tried warfarin, fondaparinux or a low molecular weight heparin product (e.g., enoxaparin, Fragmin [dalteparin injection]); OR
      Note: A patient who has tried Eliquis (apixaban tablets), Pradaxa (dabigatran capsules and oral pellets), or Savaysa (edoxaban tablets) is not required to try warfarin, fondaparinux, or a low molecular weight heparin.
      ii. Patient has been started on Xarelto for the treatment of an acute thromboembolic condition; AND
   B) If Xarelto oral suspension is being requested, approve if the patient meets one of the following (i or ii):
      i. Patient is unable to have Xarelto tablets appropriately administered; OR
      ii. The prescribed Xarelto dose cannot be achieved by Xarelto 10 mg, 15 mg, or 20 mg 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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Xarelto® tablets and oral suspension [prescribing information]. Titusville, NJ: Janssen; February 2023.
2. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease. Second update of the CHEST guideline and Expert Panel Report. *Chest*. 2021;160(6):e545-e608.
3. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO guideline update. *J Clin Oncol*. 2023;41:3063-3071.
4. The NCCN Cancer-Associated Venous Thromboembolic Disease Clinical Practice Guidelines in Oncology (version 2.2023 – June 1, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.
5. Ortel TL, Neumann I, Ageno W, Beyth R, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. *Blood Adv*. 2020;4(19):4693-4738.
6. Lip G, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report. *Chest*. 2018;154(5):1121-1201.
7. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the diagnosis and management of atrial fibrillation. A report of the American College of Cardiology/American Heart Association Joint Committee on Practice guidelines. Developed in collaboration and endorsed by the American College of Clinical Pharmacy and the Heart Rhythm Society. *J Am Coll Cardiol*. 2024;83(1):109-279.
8. Abramson BL, Al-Omran M, Anand SS, et al. Canadian Cardiovascular Society 2022 guidelines for peripheral arterial disease. *Can J Cardiol*. 2022;38:560-587.
9. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Antithrombotic therapy in patients with COVID-19. National Institutes of Health. Updated October 23, 2023. Available at: https://www.covid19treatmentguidelines.nih.gov/. Accessed on January 14, 2024.
10. Moores LK, Tritschler T, Brosnahan S, et al. Prevention, diagnosis, and treatment of VTE in patients with Coronavirus Disease 2019: CHEST Guideline and Expert Panel Report. *Chest*. 2020;158(3):1143-1163.
11. Spyropoulos AC, Levy JH, Ageno W, et al. Scientific and Standardization Committee communication: Clinical guidance on the diagnosis, prevention, and treatment of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost*. 2020;18:1859-1865.
12. Barnes GD, Burnett A, Allen A, et al. Thromboembolic prevention and anticoagulant therapy during the COVID-19 pandemic: updated clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis*. 2022;54:197-210.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Atrial Fibrillation (or Atrial Flutter):** Added Patient is ≥ 18 years of age; AND If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered.	8/1/2024

	Coronary Artery Disease: Added Patient is ≥ 18 years of age; AND If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered. **Deep Vein Thrombosis in a Patient Undergoing Knee or Hip Replacement Surgery, Prophylaxis:** Added Patient is ≥ 18 years of age; AND If Xarelto oral suspension is being requested, approve if the patient is unable to have Xarelto tablets appropriately administered. **Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence:** Added differentiation between tablets and suspension and for Xarelto oral suspension: Approve if the patient meets one of the following: Patient is unable to have Xarelto tablets appropriately administered; OR The prescribed Xarelto dose cannot be achieved by Xarelto 10 mg, 15 mg, or 20 mg tablets. **Peripheral Artery Disease:** Added Patient is ≥ 18 years of age; AND If Xarelto oral suspension is being requested, patient is unable to have Xarelto tablets appropriately administered. **Thromboprophylaxis in a Patient with Congenital Heart Disease.** Added Patient is ≥ 2 years of age and < 18 years of age **Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis.** Added Patient is ≥ 18 years of age; AND If Xarelto oral suspension is being requested, patient is unable to have Xarelto tablets appropriately administered. **Conditions Not Covered:** Removed Prophylaxis of Venous Thromboembolism in Individuals with Factor V Leiden thrombophilia and Antiphospholipid syndrome from the list of conditions. This update was for list maintenance purposes only and does not reflect any change in coverage status.	

The policy effective date is in force until updated or retired.