PRIOR AUTHORIZATION POLICY

POLICY: Anticoagulants – Xarelto Prior Authorization Policy
- Xarelto® (rivaroxaban tablets and oral suspension – Janssen)

REVIEW DATE: 01/11/2023

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.

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]

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 December 28, 2022), hospitalized patients with COVID-19 should not be routinely discharged from the hospital while on 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xarelto. All approvals are provided for the approval duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Xarelto (tablets and oral suspension) is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Atrial Fibrillation (or Atrial Flutter).** Approve for 1 year if the patient meets both of the following criteria (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 both 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 19 (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 criteria (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), 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 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Xarelto is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xarelto® tablets and oral suspension [prescribing information]. Titusville, NJ: Janssen; March 2022.
2. Guyatt GH, Akl EA, Crowther M, et al, for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:7S-47S.
3. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST Guideline and Expert Panel Report. *Chest*. 2016;149(2):315-352.
4. The NCCN Cancer-Associated Venous Thromboembolic Disease Clinical Practice Guidelines in Oncology (version 1.2022 – March 11, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 5, 2023.
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 Oct 13;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. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol.* 2019;74(1):104-132.
8. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Updated December 28, 2022. Available at: https://www.covid19treatmentguidelines.nih.gov/. Accessed on January 5, 2023.
9. 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 Sep;158(3):1143-1163.
10. 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.
11. Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis*. 2020 Jul;50(1):72-81.

NA – Not applicable.