

PRIOR AUTHORIZATION POLICY

POLICY: Anticoagulants – Xarelto Prior Authorization Policy

- Xarelto® (rivaroxaban tablets – Janssen)

REVIEW DATE: 11/18/2020; selected revision 06/16/2021

OVERVIEW

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

- **Non-valvular atrial fibrillation**, to reduce the risk of stroke and systemic embolism.
- **Prophylaxis of deep vein thrombosis (DVT)**, which may lead to pulmonary embolism (PE), in patients undergoing knee or hip replacement surgery.
- **Prophylaxis of venous thromboembolism in acutely ill medical patients** at risk for thromboembolic complications not at high risk of bleeding.
- **Reduction in risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, and stroke)**, in combination with aspirin, in patients with chronic coronary artery disease or peripheral arterial disease.
- **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.

Guidelines

Guidelines are available which support the use of direct oral anticoagulants (DOACs) in their commonly used clinical settings, such as DVT/PE²⁻⁴ and atrial fibrillation^{5,6}. 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.⁶

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. In a guideline from the American College of Chest Physicians (CHEST) [June 2, 2020], anticoagulant thromboprophylaxis is suggested over no prophylaxis for acutely ill hospitalized patients with COVID-19.⁷ Extended thromboprophylaxis after hospital discharge is not routinely recommended but may be considered for a patient with low bleeding risk, if emerging data on the post-discharge risk of venous thromboembolism (VTE) and bleeding indicate a net benefit of such prophylaxis. Randomized, controlled trials have not been conducted to evaluate the efficacy of various anticoagulants or placebo in COVID-19 patients; however, the guideline notes that most patients with COVID-19 would have been eligible to participate in landmark trials of anticoagulant thromboprophylaxis in acutely ill medical inpatients. According to guidance from the International Society of Thrombosis and Hemostasis (May 27, 2020), extended post-discharge thromboprophylaxis should be considered for all hospitalized patients with COVID-19 who meet high VTE risk criteria.⁸ Xarelto and Bevyxxa (betrixaban capsules) are cited as treatment options for extended-duration thromboprophylaxis. Likewise, guidance from the Anticoagulation Forum (May 21, 2020) states that for a COVID-19 patient in whom post-discharge prophylaxis is deemed reasonable, an adequately studied and/or approved agent such as Bevyxxa or Xarelto is recommended.

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

FDA-Approved Indications

- 1. Atrial Fibrillation (or Atrial Flutter).** Approve for 1 year.
- 2. Deep Vein Thrombosis in a Patient Undergoing Knee or Hip Replacement Surgery, Prophylaxis.** Approve for 60 days.
- 3. Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Approve for 1 year.
- 4. Deep Vein Thrombosis or Pulmonary Embolism, to Reduce the Risk of Recurrence.** Approve for 1 year.
- 5. Reduction in Risk of Major Cardiovascular Events.** Approve for 1 year if the patient meets the following criteria (A and B):
 - A)** Patient has coronary artery disease or peripheral artery disease; AND
 - B)** Patient will be taking concomitant aspirin at least 75 mg daily.
- 6. Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis.** Approve for 60 days.
Note: This includes post-discharge thromboprophylaxis for a patient hospitalized with coronavirus disease 19 (COVID-19).

Other Uses with Supportive Evidence

- 7. Treatment or Prevention of Other Thromboembolic-Related Conditions.** Approve for 6 months if the patient meets ONE of the following criteria (A or 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 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.

B) Patient has been started on Xarelto for the treatment of an acute thromboembolic condition.

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 [prescribing information]. Titusville, NJ: Janssen; March 2020.
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 1.2020—April 16, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on November 2, 2020.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.