Effective Date **6/15/2023**
Next Review Date… **6/15/2024**
Coverage Policy Number **IP0030**

Apixaban

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Related Coverage Resources

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. 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.

Overview

This policy supports medical necessity review for apixaban tablets (**Eliquis**®).

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

Medical Necessity Criteria

Apixaban (Eliquis) is considered medically necessary when there is documentation of ONE of the following:

1. **Atrial Fibrillation (or Atrial Flutter).**
2. **Deep Vein Thrombosis in Individuals Undergoing Hip or Knee Replacement Surgery, Prophylaxis.**
3. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.**

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

5. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Individual meets **ONE** 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 failure, contraindication, or intolerance to **ONE** of the following: warfarin, fondaparinux injection, a low molecular weight heparin product.
   B) Previously started on Eliquis for the treatment of an acute thromboembolic condition.

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 Apixaban (Eliquis) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration:
- Atrial Fibrillation (or Atrial Flutter): up to 12 months
- Deep Vein Thrombosis in Individuals Undergoing Hip or Knee 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
- 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
- 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):

1. **Prophylaxis of Venous Thromboembolism in Acutely Ill Individuals.** (Note: This includes post-discharge thromboprophylaxis for an individual hospitalized with coronavirus disease 19 [COVID-19]). Eliquis has been compared with enoxaparin for post-discharge prophylaxis in acutely ill medical individuals; however, superiority vs. enoxaparin was not achieved, and bleeding was increased with Eliquis.[10] Xarelto and Bevyxxa (note: Bevyxxa has been withdrawn from the market) are labeled for prophylaxis of venous thromboembolism in acutely ill medical individuals and are supported in clinical practice guidelines, including guidelines which address prophylaxis of venous thromboembolism in COVID-19 individuals.[7-9]

2. **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
Eliquis, a 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 who have undergone hip or knee replacement surgery.
- **Treatment of DVT and PE**, as well as reduction in the risk of recurrence of DVT and PE following initial therapy.

Safety and effectiveness of Eliquis in pediatric patients have not been established.[1]

Guidelines
Guidelines are available which support the use of direct oral anticoagulants (DOACs) in their commonly used clinical settings, such as DVT/PE2-5 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 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® (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.[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.

References

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