PRIOR AUTHORIZATION POLICY

POLICY: Anticoagulants – Eliquis Prior Authorization Policy
- Eliquis® (apixaban tablets and tablets for oral suspension – Bristol-Myers Squibb/Pfizer)
- Eliquis® Sprinkle (apixaban capsules for oral suspension – Bristol-Myers Squibb/Pfizer)

REVIEW DATE: 05/21/2025

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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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 NATIONAL FORMULARY COVERAGE:

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 in adults.
- **Prophylaxis of deep vein thrombosis (DVT)**, which may lead to pulmonary embolism (PE), in adults 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, in adults.
- **Treatment of VTE and reduction in the risk of recurrent VTE** in pediatric patients from birth and older at least 5 days after initial anticoagulant treatment.

It is noted in the prescribing information for Eliquis that different dosage forms can be utilized to achieve the necessary dose for pediatric patients.[1] Not all dosage forms are

approved for the same indication and age groups. Eliquis Sprinkle is available as a 0.15 mg strength and can be used for patients 2.6 to less than 4 kg. Eliquis tablets for oral suspension are available as a 0.5 mg strength and can be used for patients 4 to 35 kg. Eliquis also remains available as 2.5 and 5 mg tablets; these can be used for patients ≥ 35 kg. Eliquis/Eliquis Sprinkle are not recommended for use in pediatric patients less than 2.6 kg because it was not studied in these 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 a lower risk of serious bleeding.[7]

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 (2024) suggest anticoagulation for certain patients (e.g., superficial vein thrombosis,).[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.

POLICY STATEMENT

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

I. <u>Eliquis tablets</u> is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Atrial Fibrillation (or Atrial Flutter).** Approve for 1 year if the patient is ≥ 18 years of age.

2. **Deep Vein Thrombosis in a Patient Undergoing Hip or Knee Replacement Surgery, Prophylaxis.** Approve for 60 days if the patient is ≥ 18 years of age.

3. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Approve for 1 year if the patient weighs ≥ 35 kg.

4. **Deep Vein Thrombosis or Pulmonary Embolism to Reduce the Risk of Recurrence.** Approve for 1 year if the patient weighs ≥ 35 kg.

Other Uses with Supportive Evidence

5. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Approve for 6 months if the patient meets BOTH of the following (A <u>and</u> 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 is ≥ ≥ 35 kg; AND

B) Patient meets ONE of the following (i or ii):

- **i.** Patient has tried warfarin, fondaparinux injection, or a low molecular weight heparin product (e.g., enoxaparin injection, Fragmin [dalteparin injection]); OR
  Note: A patient who has tried Xarelto (rivaroxaban tablets and oral suspension), Pradaxa (dabigatran capsules and oral pellets), or Savaysa (edoxaban tablets) is not required to try warfarin, fondaparinux, or a low molecular weight heparin product.
- **ii.** Patient has been started on Eliquis for the treatment of an acute thromboembolic condition.

II. Eliquis tablets for oral suspension and Eliquis Sprinkle capsules for oral suspension is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Venous Thromboembolic Events, Treatment**. Approve for 1 year if patient weighs < 35 kg.
   Note: Examples of venous thromboembolic events include deep vein thrombosis, cerebral vein thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis.

2. **Venous Thromboembolic Events, To Reduce the Risk of Recurrence.** Approve for 1 year if patient weighs < 35 kg.
   Note: Examples of venous thromboembolic events include deep vein thrombosis, cerebral vein thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis.

Other Uses with Supportive Evidence

3. **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 weighs < 35 kg; AND
   B) 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 Xarelto (rivaroxaban tablets and oral suspension), Pradaxa (dabigatran capsules and oral pellets) is not required to try warfarin, fondaparinux, or a low molecular weight heparin product.
   - **ii.** Patient has been started on Eliquis tablets for oral suspension or Eliquis capsules for oral suspension for the treatment of an acute thromboembolic condition.

CONDITIONS NOT COVERED

- **Eliquis® (apixaban tablets and tablets for oral suspension - Bristol-Myers Squibb/Pfizer)**
- **Eliquis® Sprinkle (apixaban capsules for oral suspension – Bristol-Myers Squibb/Pfizer)**

is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis.** Eliquis has been compared with enoxaparin for post-discharge prophylaxis in acutely ill medical patients; however, superiority vs. enoxaparin was not achieved, and bleeding was increased with Eliquis.[10] Xarelto is labeled for prophylaxis of venous thromboembolism in acutely ill medical patients and is supported in clinical practice guidelines.

REFERENCES

1. Eliquis® tablets [prescribing information]. Princeton, NJ and New York, NY: Bristol-Myers Squibb and Pfizer; May 2025.
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*. 2024; 166(2): 388-404.
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 1.2025 – February 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 12, 2025.
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. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Antithrombotic therapy in patients with COVID-19. National Institutes of Health. Updated February 29, 2024.
9. Goldhaber SZ, Leizorovicz A, Kakkar AK, et al. Apixaban versus enoxaparin for thromboprophylaxis in medically ill patients. *N Engl J Med*. 2011;365(23):2167-2177.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	No criteria changes.	01/11/2023

Annual Revision	No criteria changes.	01/24/2024
Annual Revision	No criteria changes.	02/12/2025
Early Annual Revision	**Eliquis tablets for oral suspension and Eliquis capsules for oral suspension:** These formulations and conditions for approval were added to the policy. **Eliquis tablets:** • **Deep Vein Thrombosis or Pulmonary Embolism, Treatment:** The requirement that the patient is ≥ 18 years of age was changed to patient weighs ≥ 35 kg. • **Deep Vein Thrombosis or Pulmonary Embolism to Reduce the Risk of Recurrence:** The requirement that the patient is ≥ 18 years of age was changed to patient weighs ≥ 35 kg. • **Treatment or Prevention of Other Thromboembolic-Related Conditions:** The requirement that the patient is ≥ 18 years of age was changed to patient weighs ≥ 35 kg. For the criterion that requires a patient to try warfarin, fondaparinux, or a low molecular weight heparin product, Pradaxa oral pellets was added to the medications that a patient could alternatively try; previously only the capsule formulation of Pradaxa was listed.	05/21/2025