



Original Effective Date: 1/1/2020  
Current Effective Date: 04/2022  
Last P&T Approval/Version: 04/27/2022  
Next Review Due By: 10/2024  
Policy Number: C18476-A

## Eliquis (apixaban) - IL Medicaid Only

### PRODUCTS AFFECTED

Eliquis (apixaban)

### COVERAGE POLICY

*Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.*

#### **Documentation Requirements:**

*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive*

#### **DIAGNOSIS:**

Indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; Indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery. Indicated for the treatment of DVT; Indicated for the treatment of PE; Indicated to reduce the risk of recurrent DVT and PE following initial therapy

#### **COMPENDIAL APPROVED OFF-LABELED USES:**

Cancer-associated venous thromboembolism prophylaxis

#### **REQUIRED MEDICAL INFORMATION:**

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

#### **A. FOR ALL INDICATIONS**

1. Documentation that member has ONE of the following labeled indications for Eliquis

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## Drug and Biologic Coverage Criteria

(apixaban)

- i. Nonvalvular atrial fibrillation
- ii. Treatment of Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)
- iii. Member had a recent hip replacement (within previous 35 days) or is scheduled for a hip replacement surgery and requires DVT prophylaxis
- iv. Member had a recent knee replacement (within previous 12 days) or is scheduled for a knee replacement surgery and requires DVT prophylaxis
- v. Prophylaxis therapy to reduce the risk of recurrent DVT or PE following initial therapy

OR

2. Documentation patient has cancer other than basal-cell or squamous cell skin cancer that is active or had been diagnosed within the previous 2 years and requires treatment or prophylaxis of thromboembolism

### CONTINUATION OF THERAPY:

#### A. FOR ALL INDICATIONS

1. Documentation showing member continues to meet labeled indications or has medical necessity for prophylaxis due to cancer diagnosis  
AND
2. Dose requested is appropriate for members diagnosis

### DURATION OF APPROVAL:

Initial authorization:

Prophylaxis for Hip Replacement: 35 days

Prophylaxis for Knee Replacement: 12 days

Prophylaxis to reduce risk of recurrence after treatment of acute DVT and/or PE: 12 months

Atrial Fibrillation: 12 months

DVT or PE treatment: 6 months

Cancer-associated venous thromboembolism prophylaxis: 3 months

Continuation of Therapy (for the following indications only): Prophylaxis to reduce risk of recurrence after treatment of acute DVT and/or PE, Atrial Fibrillation, Cancer-associated venous thromboembolism prophylaxis, DVT or PE treatment: 12 months

### PRESCRIBER REQUIREMENTS:

None

### AGE RESTRICTIONS:

18 years of age and older

### QUANTITY:

Treatment of DVT or PE: 10 mg PO twice daily for 7 days, followed by 5 mg PO twice daily for at least 6 months

Atrial Fibrillation: 5 mg twice daily

DVT and PE prophylaxis: 2.5 mg twice daily x 6 months

DVT and PE prophylaxis following hip replacement: 2.5 mg twice daily for 35 days

DVT and/or PE prophylaxis following knee surgery: 2.5 mg twice daily for 12 days

Cancer-Associated venous thromboembolism prophylaxis: 2.5 mg twice daily

The recommendation is that oral and injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

## DRUG INFORMATION

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**ROUTE OF ADMINISTRATION:**

Oral

**DRUG CLASS:**

Direct Factor Xa Inhibitors Oral

**FDA-APPROVED USES:**

Indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; Indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery.; Indicated for the treatment of DVT; Indicated for the treatment of PE; Indicated to reduce the risk of recurrent DVT and PE following initial therapy

**COMPENDIAL APPROVED OFF-LABELED USES:**

Cancer-associated venous thromboembolism prophylaxis

**APPENDIX**

**APPENDIX:**

Reference: NCCN Clinical Practice Guidelines in Oncology, Cancer-Associated Venous Thromboembolism Disease, Version 1.2022, April 15, 2022, NCCN.org

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**NCCN** National Comprehensive Cancer Network® **NCCN Guidelines Version 1.2022** **Cancer-Associated Venous Thromboembolic Disease** [NCCN Guidelines Index](#) [Table of Contents](#) [Discussion](#)

**VTE PROPHYLAXIS OPTIONS FOR AMBULATORY MEDICAL ONCOLOGY PATIENTS (VTE-2)<sup>1</sup>**

Agent	Standard Dosing	Renal Dose	Other Dose Modifications
Apixiban <sup>11</sup>	2.5 mg PO twice daily	Avoid if CrCl <30 mL/min	Avoid if platelet count <50,000/µL Avoid if weight <40 kg
Rivaroxaban <sup>9,12</sup>	15 mg PO once daily	Avoid if CrCl <30 mL/min	Avoid if platelet count <50,000/µL
Dabigatran <sup>13</sup>	200 units/kg SC daily x 1 month, then 150 units/kg SC daily x 2 months	Avoid if CrCl <30 mL/min	Avoid if platelet count <50,000/µL Avoid if weight <40 kg
Enoxaparin <sup>14</sup>	1 mg/kg SC daily x 3 months, then 40 mg SC daily	Avoid if CrCl <30 mL/min	Reduce dose to 0.5 mg/kg SC daily for platelet count 30,000–75,000/µL  Avoid if platelet count <50,000/µL

CrCl = estimated creatinine clearance; PO = oral; SC = subcutaneous

<sup>11</sup> Recommendations derived from clinical trials of high thrombosis risk ambulatory cancer patients (>16 years, Khawaja VTE Risk Score of ≥2, initiating new course of chemotherapy) and are not included in product labeling. Prophylaxis duration should be 6 months or longer if risk persists.

<sup>12</sup> For recommendations for thromboprophylaxis in multiple myeloma patients, see [NCCN Guidelines for Multiple Myeloma](#).

<sup>13</sup> Absorption is affected in the stomach, proximal small bowel, and colon. Patients who have had significant resections of these portions of the intestinal tract may be at risk for suboptimal absorption.


<sup>14</sup> EPCAs are absorbed primarily in the stomach and proximal small bowel, so they may not be appropriate for patients who have had significant resections of these portions of the intestinal tract.

<sup>15</sup> Data support the use of prophylactic dabigatran and enoxaparin for patients with advanced unresectable and metastatic pancreatic cancer (Nawroys A. *Cur J Cancer* 2012;46:1263-1272; Polun P, et al. *J Clin Oncol* 2013;31:2028-2034).

Note: All recommendations concerning VTE unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any patient with cancer is a clinical trial. Participation in clinical trials is especially encouraged.

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**Cancer-Associated Venous Thromboembolic Disease**

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**THERAPEUTIC ANTICOAGULATION FOR VENOUS THROMBOEMBOLISM (CONTINUED)**

**DOACs (preferred for patients without gastric or gastroesophageal lesions)<sup>1</sup>**

- Apixaban (category 1)<sup>2</sup>
  - 15 mg PO every 12 hours for 7 days followed by 5 mg PO every 12 hours<sup>1,2,15,20,21</sup>
- Edoxaban (category 1)
  - Initial therapy with LMWH<sup>3,4</sup> or UFH<sup>5,6</sup> for at least 5 days followed by edoxaban 60 mg PO daily (or 30 mg PO daily in patients with Cockcroft-Gault estimated CrCl 30–50 mL/min or weight <60 kg or concomitant potent p-glycoprotein inhibitors)<sup>6,9,17,24</sup>
- Rivaroxaban
  - 15 mg PO every 12 hours for the first 21 days followed by 20 mg daily<sup>9–11</sup>

**LMWH (preferred for patients with gastric or gastroesophageal lesions)**

- Dalteparin (category 1)
  - 200 units/kg SC daily for 30 days, then switch to 100 units/kg once daily<sup>1,4,16,17</sup>
- Enoxaparin
  - 1 mg/kg SC every 12 hours (can consider decreasing intensity to 1.5 mg/kg daily after first month)<sup>9,15,20</sup>

**DOACs (if above regimens not appropriate or unavailable)<sup>8</sup>**

- Dabigatran
  - Initial therapy with LMWH<sup>3,4</sup> or UFH<sup>5,6</sup> for at least 5 days followed by dabigatran 150 mg PO every 12 hours<sup>4,21,22</sup>

**Fondaparinux<sup>22,26</sup>**

- 6 mg SC daily (<50 kg)
- 7.5 mg SC daily (50–100 kg)
- 10 mg SC daily (>100 kg)

**UFH (category 2B)<sup>5</sup>**

- IV 60 units/kg bolus, followed by 18 units/kg/h adjusted to target aPTT of 2–2.5 X control or per hospital SOPs, followed by SC 250 units/kg every 12 hours (category 2B)
- SC 333 units/kg load, followed by 250 units/kg every 12 hours<sup>28</sup>

**Warfarin<sup>1,19,28</sup>**

- Start warfarin concurrently with LMWH, fondaparinux, or UFH (see dosing below)
- Warfarin 5 mg daily adjusted to INR 2–3 (2.5 mg daily initial dose for liver disease or use with interacting medications)

**+ LMWH<sup>3,4</sup> + warfarin<sup>1,9</sup> options:**

- Dalteparin 200 units/kg SC daily<sup>4</sup> or 100 units/kg SC every 12 hours
- Enoxaparin 1 mg/kg SC every 12 hours<sup>1</sup>

**+ Fondaparinux + warfarin<sup>9,20,24</sup>**

- 6 mg SC daily (<50 kg)
- 7.5 mg SC daily (50–100 kg)
- 10 mg SC daily (>100 kg)

**+ UFH<sup>5</sup> + warfarin<sup>9</sup> options:**

- IV 60 units/kg bolus, followed by 18 units/kg/h adjusted to target aPTT of 2–2.5 X control or per hospital SOPs
- SC 333 units/kg load, followed by 250 units/kg every 12 hours

<sup>1</sup> Patients with gastric and gastroesophageal tumors are at increased risk for hemorrhage with DOACs.

<sup>2</sup> Apixaban may be safer than edoxaban or rivaroxaban for patients with gastric or gastroesophageal lesions (category 2B).

<sup>3</sup> LMWH dosing options: Dalteparin 200 units/kg SC daily; Enoxaparin 1 mg/kg SC every 12 hours.

<sup>4</sup> UFH dosing options: IV 60 units/kg bolus, followed by 18 units/kg/h, adjusted to a target aPTT of 2–2.5 X control or per hospital SOPs; SC 333 units/kg load, followed by 250 units/kg every 12 hours.

<sup>5</sup> Unlike warfarin, concurrent administration with parenteral anticoagulants is not recommended when transitioning to edoxaban or dabigatran. See prescribing information for protocols for transitioning between agents.

<sup>6</sup> Although each of the LMWH agents has been studied in randomized controlled trials in patients with cancer, the efficacy of dalteparin in this population is supported by the highest quality evidence and is the only LMWH approved by the FDA for this indication.

<sup>9</sup> Long-term management with enoxaparin dosing of 1 mg/kg SC every 12 hours has not been tested in patients with cancer.

<sup>11</sup> If warfarin is selected for chronic anticoagulation, initiate warfarin concurrently with the parenteral agent used for acute therapy and continue both therapies for at least 5 days and until INR is 2. During the transition to warfarin monotherapy, the INR should be measured at least twice weekly. Once the patient is on warfarin alone, the INR should be measured initially at least once weekly. Once the patient is on a stable dose of warfarin with an INR of 2–3, INR testing can be gradually decreased to a frequency of no less than once a month.

Note: All recommendations are category 2B, unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

**References**

VTE-D  
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**BACKGROUND AND OTHER CONSIDERATIONS**

**BACKGROUND:**  
None

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**  
All other uses of Eliquis (apixaban) are considered experimental/investigational and therefore, will follow Molina’s Off- Label policy. Contraindications to Eliquis (apixaban) include: Active pathological bleeding and Severe hypersensitivity reaction to Eliquis (apixaban).

**OTHER SPECIAL CONSIDERATIONS:**  
Eliquis is not recommended for use with prosthetic heart valves. There is an increased risk of thrombosis in patients with riple Positive Antiphospholipid Syndrome, therefore, ELIQUIS use not recommended. Additionally, use of Eliquis is not recommended during pregnancy or lactation. Eliquis is not recommended with severe hepatic impairment.

**CODING/BILLING INFORMATION**

**AVAILABLE DOSAGE FORMS:**  
Eliquis DVT/PE Starter Pack TBPK 5MG  
Eliquis TABS 2.5MG  
Eliquis TABS 5MG

**REFERENCES**

1. ELIQUIS® (apixaban) Package Insert. Bristol-Myers Squibb Company, Princeton, NJ, and Pfizer Inc, New York, NY. 09/2021
2. NCCN Clinical Practice Guidelines in Oncology, Cancer-Associated Venous Thromboembolism Disease, Version 1.2022, April 15, 2022, NCCN.org
3. Illinois HFS Drugs with Stipulated PA Language per Contract for MCOs 10.01.2023, revised.

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q2/2022
<b>ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.</b>	10/2023