Eliquis (apixaban)
Policy Number: C15354-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
11/2018	6/17/2020	6/17/2021
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J3490 (NOC)	RxPA	Q3 2020 20200722C15354-A

PRODUCTS AFFECTED:
Eliquis (apixaban)

DRUG CLASS:
Direct Factor Xa Inhibitors Oral

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Retail Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and member self-administered

AVAILABLE DOSAGE FORMS:
Eliquis 2.5 mg, Eliquis 5 mg, Eliquis 5 mg 30-day starter pack

FDA-APPROVED USES:
indicated: to reduce the risk of stroke and systemic embolism in members with non-valvular atrial fibrillation, for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in members who have undergone hip or knee replacement surgery. And for the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy.

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
atrial fibrillation, deep vein thrombosis treatment and prophylaxis, pulmonary embolism treatment and prophylaxis, stroke prophylaxis

REQUIRED MEDICAL INFORMATION:
FOR ALL INDICATIONS:

1. Prescriber attests that member is not currently pregnant and does not plan on becoming pregnant
   AND

2. IF THIS NON-FORMULARY PRODUCT: Documentation of trial and failure or absolute contraindication to preferred formulary Direct Factor Xa Inhibitors Oral products

A. NONVALVULAR ATRIAL FIBRILLATION:
1. Documentation of diagnosis with non-valvular atrial fibrillation or flutter of < 48 hours duration
   AND
2. Prescriber attests that patient has moderate to high risk for stroke based on the patient'sCHA2DS2-VASc score used to assess patient's stroke risk.
   AND
3. Member does NOT have moderate to severe mitral stenosis, mechanical prosthetic valves or bioprosthetic valves- If member DOES have moderate to severe mitral stenosis, mechanical prosthetic valves or bioprosthetic valves, warfarin MUST be used as the anticoagulant
   AND
4. Prescriber attests that member's renal function (creatinine clearance) will be assessed as clinically indicated and therapy will be adjusted accordingly.

B. TREATMENT OF DVT AND/OR PE:
1. Documentation of diagnosis of a DVT or PE

C. PROPHLAXIS OF DVT:
1. Member has or is scheduled to have total knee replacement surgery
   OR
2. Member has or is scheduled to have total hip replacement surgery
   OR
3. Documentation member is at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least 6 months

E. CONTINUATION OF THERAPY UPON HOSPITAL DISCHARGE:
1. Documentation of recent hospital discharge (within 48 hours) in which Eliquis was started as an in-member

F. CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM:
1. Prescriber attests that member has an acute symptomatic or incidentally detected deep-vein thrombosis
   AND
2. Documentation member has cancer other than basal-cell or squamous cell skin cancer that is active or had been diagnosed within the previous 2 years

DURATION OF APPROVAL:
Initial authorization: Prophylactic use DVT and/or PE knee – 12 days Prophylactic use DVT and/or PE hip replacement -- 35 days, Prophylactic use DVT and/or PE after treatment for acute DVT and/or PE-- 6 months, atrial fibrillation, deep vein thrombosis, pulmonary embolism treatment -- 6 months, Stroke prophylaxis – 12 months, Cancer-Associated venous thromboembolism: 3 months

Continuation of Therapy(for the following indications ONLY): Prophylactic use DVT and/or PE after treatment for acute DVT and/or PE, atrial fibrillation, deep vein thrombosis, pulmonary embolism treatment or stroke prophylaxis: 12 months, Cancer-Associated venous thromboembolism:12 months

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
Stroke prophylaxis: 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: 10mg twice daily for 7 days, then 5mg twice daily

PRESCRIBER REQUIREMENTS:
No requirements

AGE RESTRICTIONS:
18 year of age and older

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:
1. Documentation of tolerability of therapy
   AND
2. Documentation showing continued medical necessity for indication and/or medical history.
   AND
3. Dosing is appropriate for listed diagnosis.
   AND
4. Compliance with therapy as verified by Prescriber and member's medication fill history (review member's prescription history for compliance). Therapy may be discontinued due to compliance issues or poor adherence upon agreement among treating physician, member, and Medical Director

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:
None

BACKGROUND:
None

APPENDIX:

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2019
Cancer-Associated Venous Thromboembolic Disease

NCCN Guidelines Index
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Discussion

THERAPEUTIC ANTICOAGULATION FOR VENOUS THROMBOEMBOLISM

- Anticoagulation options recommended for management of VTE in patients with cancer include regimens involving only one agent (monotherapy) as well as regimens that use more than one type of agent (combination therapy: VTE-E 2 of 5 and VTE-E 3 of 5). This section lists the recommended regimens, including dosing and duration, as well as a list of contraindications and warnings to help guide treatment selection.[1]
- Select regimen based on: Renal failure (CrCl <30 mL/min), inpatient/outpatient, FDA approval, cost, ease of administration, monitoring, bleeding risk assessment, and ability to reverse anticoagulation. (See Contraindications and Warnings on VTE-E 4 of 5).
- Baseline laboratory testing: CBC, renal and hepatic function panel, aPTT, and PT/INR.
- Follow institutional standard operating procedures (SOPs) for dosing schedules. If no SOPs then use the American College of Chest Physicians (ACCP) recommendations.[2]
- Following initiation of anticoagulant: Hemoglobin, hematocrit, and platelet count at least every 2–3 days for the first 14 days and every 2 weeks thereafter or as clinically indicated.

Monotherapy Options

Agent(s)	Dosing Details[a]
LMWH	
• Dalteparin (category 1)	200 units/kg SC daily for 30 days, then 150 units/kg once daily for 2–6 months[b,3,4]
• Enoxaparin	1 mg/kg SC every 12 hours[c,5-8]
Rivaroxaban	15 mg orally BID for 21 days, then 20 mg daily[9-12]
Fondaparinux	5 mg [<50 kg]; 7.5 mg [50–100 kg]; 10 mg [>100 kg] SC daily[13,14]
Unfractionated heparin (UFH) (category 2B)	
• UFH IV then SC	IV 80 units/kg load, then 18 units/kg/h, target aPTT of 2–2.5 x control or per hospital SOPs, *then SC 250 units/kg every 12 hours*[15]
• UFH SC	SC 333 unit/kg load, then SC 250 units/kg every 12 hours[15,16]
For patients who refuse or have compelling reasons to avoid LMWH,[d] the following DOACs may be acceptable alternatives for management of VTE:	
• Apixaban	10 mg orally BID for 7 days, then 5 mg BID[17,18]

[a] For recommended duration, see Duration of Anticoagulation as Recommended by Guideline on VTE-E, 3 of 5.
[b] Although each of the LMWH agents has been studied in randomized controlled trials in cancer patients, 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.[3,19]
[c] Long-term management with enoxaparin dosing of 1 mg/kg SC every 12 hours has not been tested in cancer patients.
[d] Patients may refuse or be poor candidates for LMWH injections because they are painful, inconvenient, and expensive. These factors may contribute to poor compliance with long-term LMWH treatment.

Note: All recommendations are category 2A 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-E

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, member 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.

REFERENCES:

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3. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med 2017;377:1319-30
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7. Eliquis [package insert]. Princeton, New Jersey: Bristol-Myers Squibb Company; November 2019.