Clinical Policy: Rivaroxaban (Xarelto)

Reference Number: CP.PMN.247
Effective Date: 09.01.20
Last Review Date: 08.23
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Rivaroxaban (Xarelto®) is a factor Xa inhibitor.

FDA Approved Indication(s)

Xarelto is indicated:

- To reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF).
- For the treatment of deep venous thrombosis (DVT).
- For the treatment of pulmonary embolism (PE).
- For the 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 lasting at least 6 months.
- For the prophylaxis of DVT, which may lead to PE in patients who have undergoing knee or hip replacement surgery.
- For the prophylaxis of venous thromboembolism (VTE) and VTE related death during hospitalization and post hospital discharge in adult patients admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE and not at high risk of bleeding.
- In combination with aspirin, to reduce the risk of major cardiovascular events (cardiovascular death, myocardial infarction and stroke) in patients with chronic coronary artery disease.
- In combination with aspirin, to reduce the risk of major thrombotic vascular events (myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of a vascular etiology) in patients with peripheral artery disease (PAD), including patients who have recently undergone a lower extremity revascularization procedure due to symptomatic PAD.
- For the treatment of venous thromboembolism (VTE) and the reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years after at least 5 days of initial parenteral anticoagulant treatment.
- For thromboprophylaxis in pediatric patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Xarelto is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. All FDA-approved Indications (must meet all)**:**

1. Prescribed for one of the following conditions (a - i):
   a. Reduction of the risk of stroke and systemic embolism in member with NVAF;
   b. Treatment and risk reduction of DVT or PE;
   c. Prophylaxis of DVT or PE in those who have undergone knee or hip replacement surgery;
   d. Reduction of the risk of recurrence of DVT and/or PE in adult patients at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at last 6 months;
   e. Continuation of VTE prophylaxis following hospital discharge and member was admitted for an acute medical illness at risk for thromboembolic complications;
   f. To reduce the risk of major cardiovascular events (cardiovascular death, myocardial infarction and stroke) in patients with chronic coronary artery disease (CAD) and prescribed in combination with aspirin;
   g. To reduce the risk of major thrombotic vascular events in patients with PAD, including patients after recent lower extremity revascularization due to symptomatic PAD;
   h. Treatment of VTE and risk reduction of recurrent VTE in pediatric patients < 18 years after at least 5 days of initial parenteral anticoagulant treatment;
   i. Thromboprophylaxis in pediatric patients aged ≥ 2 years with congenital heart disease who have undergone the Fontan procedure;
2. For requests in conditions a, b, c, and d (above): Failure of Eliquis® used for ≥ 30 days at up to maximally indicated doses, unless both are contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All FDA-approved Indications (must meet all)**:**

1. Member meets one of the following (a or b):

a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed maximum dose indicated in Section V.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAD: coronary artery disease
CrCl: creatinine clearance
DVT: deep venous thrombosis
FDA: Food and Drug Administration
NVAF: non-valvular atrial fibrillation
PAD: peripheral artery disease
PE: pulmonary embolism
VTE: venous thromboembolism

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Eliquis® (apixaban)	**NVAF** 5 mg PO BID	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Prophylaxis of DVT Following Hip or Knee Replacement Surgery 2.5 mg PO BID **Treatment of DVT/PE** 10 mg PO BID for 7 days, then 5 mg PO BID **Reduction in Risk of Recurrent DVT/PE** 2.5 mg PO BID	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Active pathological bleeding
  - Severe hypersensitivity reaction to Xarelto
- Boxed warning(s):
  - Premature discontinuation of Xarelto increases the risk of thrombotic events.
  - Spinal/epidural hematoma may occur in patients treated with Xarelto who are receiving neuraxial anesthesia or undergoing spinal puncture.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NVAF	15 mg or 20 mg PO QD	20 mg/day
Treatment of DVT and PE	15 mg PO BID for the first 21 days, followed by 20 mg PO QD for the remaining treatment	See dosing regimen
Reduction in the risk of recurrence of DVT and PE	10 mg PO QD	10 mg/day
Prophylaxis of DVT and PE following hip replacement surgery	10 mg PO QD	10 mg/day
Prophylaxis of VTE in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding	10 mg PO QD in hospital and after discharge for a total recommended duration of 31 to 39 days	10 mg/day
Reduction of risk of major cardiovascular events in CAD	2.5 mg PO BID in combination with aspirin 75-100 mg PO QD	5 mg/day

Indication	Dosing Regimen	Maximum Dose
Reduction in the risk of major thrombotic vascular events in PAD, including patients after lower extremity revascularization due to symptomatic PAD	2.5 mg PO BID in combination with aspirin 75-100 mg once daily	5 mg/day
Treatment of VTE and risk reduction of recurrent VTE in pediatric patients	*Oral suspension only* 2.6 kg to 2.9 kg: 0.8 mg TID 3 kg to 3.9 kg: 0.9 mg TID 4 kg to 4.9 kg: 1.4 mg TID 5 kg to 6.9 kg: 1.6 mg TID 7 kg to 7.9 kg: 1.8 mg TID 8 kg to 8.9 kg: 2.4 mg TID 9 kg to 9.9 kg: 2.8 mg TID 10 kg to 11.9 kg: 3 mg TID 12 kg to 22.9 kg: 5 mg BID *Oral suspension or tablets* 30 kg to 49.9 kg: 15 mg QD ≥ 50 kg: 20 mg QD	20 mg/day
Thromboprophylaxis in pediatric patients with congenital heart disease	*Oral suspension only* 7 kg to 7.9 kg: 1.1 mg BID 8 kg to 9.9 kg: 1.6 mg BID 10 kg to 11.9 kg: 1.7 mg BID 12 kg to 19.9 kg: 2 mg BID 20 kg to 29.9 kg: 2.5 mg BID 30 kg to 49.9 kg: 7.5 mg QD *Oral suspension or tablets* ≥ 50 kg: 10 mg QD	10 mg/day

VI. Product Availability

- Tablet: 2.5 mg, 10 mg, 15 mg, 20 mg
- Oral suspension: 1 mg/mL

VII. References

1. Xarelto Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; February 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022406s041lbl.pdf. Accessed April 20, 2023.
2. Ortel TL, Neumann I, Ageno W, 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created based on July SDC decision and prior clinical guidance.	07.20.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.03.21	08.21
RT4: added newly FDA-approved indication for reduction of risk of major thrombotic vascular events in patients with PAD.	09.15.21	
RT4: added newly FDA-approved pediatric VTE and thromboprophylaxis in pediatric patients with congenital heart disease and new oral suspension formulation.	01.10.22	
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
3Q 2023 annual review: added "reduction in the risk of recurrence of DVT and/or PE in patients at continued risk for DVT and/or PE" in initial criteria to align with all FDA approved indications and require trial of preferred Eliquis agent; references reviewed and updated.	04.20.23	08.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right

to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.