CENTENE Corporation

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 1 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding results. 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.

Description:	Rivaroxaban (Xarelto®) is an orally bioavailable factor Xa inhibitor that selectively blocks the active site of factor Xa and does not require a cofactor (eg, antithrombin III) for activity. Activation of factor X to factor Xa via the intrinsic and extrinsic pathways plays a central role in the cascade of blood coagulation.
Brand:	Rivaroxaban (Xarelto®) 10 mg, 15mg, and 20mg tablets
FDA Labeled Indications:	For prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE) in patients undergoing knee or hip replacement surgery. For treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and/or PE. For stroke prophylaxis and systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation.

Centene Medical Policy Statements represent technical documents developed by the Medical Management Staff. Questions regarding interpretation of these policies for the purposes of benefit coverage should be directed to a Medical Management Staff person.

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 2 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

Criteria for Approval:

For DVT prophylaxis:
Ordered for post-operative DVT prophylaxis in patients who undergo knee or hip replacement surgery.

NOTE: Xarelto® 10 mg. is on the PDL with a quantity restriction of 35 tablets/6 months for knee and hip replacement surgery DVT prophylaxis.

For stroke prophylaxis and systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation; OR for treatment or reduction of risk of recurrent deep vein thrombosis (DVT) or pulmonary embolism (PE):
Trial and failure of warfarin, up to maximum doses (unless contraindicated).

Trial and failure encompasses use of warfarin with adequate titration to achieve therapeutic INR ranges and experience an ischemic event OR cannot achieve consistently therapeutic INR. OR

Clinically unacceptable risk with a change in therapy to a preferred drug

Approval Duration – Up to 6 Months

Black Box Warning:

Contraindications encompass intolerance, adverse effects or hypersensitivity that precludes the member from further treatment with warfarin.

Discontinuation in patients with nonvalvular atrial fibrillation: Premature discontinuation of any oral

anticoagulant, including rivaroxaban, increases the risk of thrombotic events. If anticoagulation with rivaroxaban is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

Approval: Approval Duration – Up to 6 months

Deep vein thrombosis prophylaxis: For prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism in patients undergoing knee or hip replacement surgery.

Deep vein thrombosis treatment: For treatment of DVT.
Nonvalvular atrial fibrillation: To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Pulmonary embolism treatment: For treatment of pulmonary embolism.

Reduction in the risk of recurrence of deep vein thrombosis and pulmonary embolism: For reduction in the risk of recurrence of DVT and pulmonary embolism following initial 6 months of treatment for DVT and/or pulmonary embolism

Administer the 15 and 20 mg tablets with food; the 10 mg tablet can be administered with or without food. For nonvalvular atrial fibrillation, administer with the evening meal.

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 4 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

Adults:
Deep vein thrombosis prophylaxis: Usual dosage: 10 mg once daily. Initial dose should be at least 6 to 10 hours after surgery once hemostasis has been established.

Duration of therapy:
Hip replacement surgery: 35 days is recommended.1 The 2012 American College of Chest Physicians (ACCP) antithrombotic guidelines recommend a minimum of 12 to 14 days, with an extended duration of 35 days suggested.
Knee replacement surgery: 12 days is recommended.1 The 2012 ACCP antithrombotic guidelines recommend a minimum of 10 to 14 days, with an extended duration of 35 days suggested.

Deep vein thrombosis treatment: Initial dosage: 15 mg twice daily with food for 21 days. Maintenance dosage: 20 mg once daily with food. Nonvalvular atrial fibrillation: 20 mg once daily with evening meal.

Pulmonary embolism treatment: Initial dosage: 15 mg twice daily with food for 21 days. Maintenance dosage: 20 mg once daily with food. Reduction in the risk of recurrence of deep vein thrombosis and/or pulmonary embolism: 20 mg once daily with food.

Children: Safety and effectiveness have not been established.

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 5 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

Deep vein thrombosis treatment/pulmonary embolism treatment/reduction in the risk of recurrence of deep vein thrombosis and/or pulmonary embolism:
Creatinine clearance less than 30 mL/min: Avoid use
Nonvalvular atrial fibrillationCreatinine clearance 15 to 50 mL/min: 15 mg once daily with evening meal.

Special Instructions

- Please refer to prescribing information for dosing, precautions, and other clinical information.
- Drug-disease interactions: Patients with impaired renal function who receive rivaroxaban with drugs that are combined weak or moderate CYP3A4 and P-gp inhibitors (eg, amiodarone, azithromycin, diltiazem, dronedarone, erythromycin, felodipine, quinidine, ranolazine, verapamil) may have increases in rivaroxaban exposure compared with patients with normal renal function and no inhibitor use because both pathways of rivaroxaban elimination are affected. While increases in rivaroxaban exposure can be expected under such conditions, results from a study did not show an increase in bleeding in patients with CrCl 30 to less than 50 mL/min.
- BBW: Patients who take anticoagulant agents are at risk of developing an epidural or spinal hematoma if they undergo neuraxial anesthesia or spinal puncture, which could result in paralysis.
- Rivaroxaban increases the risk of serious and fatal bleeding, and should not be used in patients with a history of serious bleed.
- Avoid use in moderate (Child-Pugh class B) or severe (Child-Pugh class C) hepatic impairment or any hepatic disease associated with coagulopathy.
- Use should be avoided in patients with severe renal impairment (CrCl<30 ml/min) or in ESRD requiring hemodialysis.
- Use should be avoided in patients with moderate to severe hepatic impairment (Child-Pugh B or C) or with hepatic disease associated with coagulopathy.

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 6 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

- Pregnancy Category C risk –use with caution in pregnant women due to potential for obstrectic hemorrhage and/or emergent delivery.
- Nursing Mothers – discontinue drug or discontinue nursing.
- Rivaroxaban should not be taken concomitantly with drugs that are strong inducers or inhibitors of BOTH CYP3A4 and p-glycoprotein.
- Not recommended for patients who are lactose intolerant due to formulation
- If a dose is not taken at the scheduled time, administer the dose as soon as possible on the same day. For patients receiving 15 mg twice daily, the patient should take rivaroxaban immediately to ensure intake of rivaroxaban 30 mg/day. In this particular instance, two 15 mg tablets may be taken at once. The patient should continue with the regular 15 mg twice daily intake as recommended on the following day. For patients receiving 10, 15, or 20 mg once daily, the patient should take the missed dose immediately.

References:

1. Xarelto® prescribing information. Accessed, December, 2012. http://www.xareltohcp.com/sites/default/files/pdf/xarelto_0.pdf#zoom=100
2. Xarelto® Drug Monograph. Micromedex, accessed December, 2012.
3. Xarelto® Drug Monograph. Clinical Pharmacology, accessed December, 2012.
4. Up-to-date – Xarelto®, accessed December, 2012.
5. Xarelto® prescribing information. Accessed, January, 2014.

Revision Log	
Revision	**Date**

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 7 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

FDA Labeled indications: (1) Removed wording "postoperative", "arthroplasty of the". Added (DVT), (PE). Added new indication (3) For treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) and for the reduction in the risk of recurrent DTV and/or PE.	02/13
Criteria for Approval: Added new indications "OR for treatment or reduction of risk of recurrent DVT/PE:";	02/13
Under initial approval added indication for nonvalvular atrial fibrillation/prevention of recurrent DVT/PE. Added wording "once daily for". Added "Initial Approval treatment of DVT/PE: 15mg BID for 21 days then 20mg once daily for 6 months. Added the continued approval 12 months (to reduce risk of recurrent DVT/PE). Changed wording on the "NOTE" replaced approvable with "the maximum recommended dose".	02/13
Special Instructions: added "in ESRD requiring hemodialysis." To renal warning; put warning for hepatic impairment on separate line; changed pregnancy warning from "not recommended" to "use with caution in pregnant women due to potential for obstrectic hemorrhage and/or emergent delivery." Added "Nursing Mothers – discontinue drug or discontinue nursing."	02/13
Updated references to reflect current literature search.	02/13
Addition of "Black box warning"	02/14
Revision of approvals and current literature search	02/14
Updating indication to the package insert August 2013	02/14
Updated references.	02/15
A. Added Clinically unacceptable risk with a change in therapy to a preferred drug	06/15
Added approval duration of up to 6 months. Information regarding renal function removed as this does not affect approval or denial decision	5/16

PRIOR AUTHORIZATION GUIDELINE

DEPARTMENT: Pharmacy	**DOCUMENT NAME:** rivaroxaban (Xarelto®)
PAGE: 8 of 8	**REFERENCE NUMBER:** NH.PPA.13
EFFECTIVE DATE: 02/12	**REPLACES DOCUMENT:**
RETIRED:	**REVIEWED:** 03/17
PRODUCT TYPE: Medicaid	**REVISED:** 02/13, 02/14, 02/15, 5/16

Annual Review, No Changes	03/17

POLICY AND PROCEDURE APPROVAL

Pharmacy & Therapeutics Committee: Approval on file

V.P., Pharmacy Operations: Approval on file

Sr. V.P., Chief Medical Officer: Approval on file

NOTE: The electronic approval is retained in Compliance 360.