

Rivaroxaban (XARELTO) LOW-DOSE (2.5 mg twice daily) Criteria for Use in Chronic Coronary Artery Disease (CAD) June 2022

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph Addendum on this drug at the [PBM INTERnet](#) or [PBM INTRAnet](#) site for further information.

NOTE: This document provides clinical guidance for the use of LOW-DOSE (2.5 mg twice daily) rivaroxaban plus aspirin ONLY in the setting of CHRONIC, STABLE CAD.

- **Additional PBM guidance is available for the use of rivaroxaban for its other indications (see <https://vaww.cmopnational.va.gov/cmop/PBM/default.aspx/>):**
 - Direct Oral Anticoagulants (DOAC) CFU and Algorithm for Nonvalvular Atrial Fibrillation
 - DOAC CFU and Algorithm for VTE Treatment
 - DOAC CFU for VTE prophylaxis in Orthopedic Surgery
 - DOAC CFU for Peripheral Arterial Disease (PAD)

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive LOW-DOSE (2.5 mg twice daily) rivaroxaban.

- Indication for non-aspirin antiplatelet therapy including dual antiplatelet therapy (e.g., aspirin plus clopidogrel, ticagrelor, or prasugrel)
- Indication for therapeutic dose of an oral anticoagulant (e.g., atrial fibrillation, venous thromboembolism treatment, etc.)
- Recent stroke (within past 30 days) or any history of hemorrhagic stroke
- Heart failure (ejection fraction [EF] less than 40% or NYHA class III or IV symptoms)
- Estimated glomerular filtration rate (eGFR) less than 15 ml/min
- Known hepatic disease associated with coagulopathy
- Concurrent use of combined P-glycoprotein and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin)
- Concurrent use of combined P-glycoprotein and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir and ritonavir combinations, cobicistat)
- Pregnancy
- Breastfeeding
- High risk of bleeding per clinician discretion*

*There was a significantly higher risk of major bleeding with rivaroxaban plus aspirin vs. aspirin alone in a population of stable CAD patients not at a high risk of bleeding

Inclusion Criteria

The answer to the following must be fulfilled in order to meet criteria

- Prescribed low dose aspirin (75 to 100 mg) once daily as indicated for use with rivaroxaban LOW-DOSE (2.5 mg twice daily)

Additional Inclusion Criteria

One of the following must be checked for patient to be eligible:

- Documented myocardial infarction in the past 20 years
- Multivessel coronary disease** with symptoms or with history of angina (stable or unstable)
- Multivessel percutaneous coronary intervention
- Multivessel coronary artery bypass graft (CABG) surgery

**Multivessel coronary disease was defined in the COMPASS trial as stenosis of 50% or more in 2 or more coronary arteries or in 1 coronary territory if at least 1 other territory has been revascularized

Additional Inclusion Criteria

One of the following must be checked for patient to be eligible:

- Age 65 years or older
- Less than 65 years old and documented atherosclerosis or revascularization in two vascular beds (coronary vascular bed plus one additional vascular bed - e.g., aorta, brain, gastrointestinal tract, limbs, kidneys)
- Less than 65 years old with two or more risk factors: current smoker (within the last year); diabetes; renal impairment (estimated glomerular filtration rate [GFR] less than 60 mL/min); atherosclerotic ischemic stroke at least one month ago

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