Direct Oral Anticoagulants (DOACs)
Dabigatran (PRADAXA), Rivaroxaban (XARELTO), Apixaban (ELIQUIS), and Edoxaban (SAVAYSA)
Criteria for Use
December 2023

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.

Exclusion Criteria

The following must be met.

☐ Patient has no exclusions to receiving a DOAC (exclusions are listed below)

- Mechanical heart valve
- Moderate to severe rheumatic mitral valve stenosis (for patients with atrial fibrillation/flutter only)
- Antiphospholipid syndrome (APS). DOACs have been shown to be less effective than warfarin in preventing arterial thrombosis in patients with APS, and warfarin is favored in most APS patients.
- Known significant liver disease (e.g. acute clinical hepatitis, cirrhosis [Child-Pugh C]), or hepatic disease associated with coagulopathy^1
- Pregnancy
- Breastfeeding

Inclusion Criteria

ONE of the following must be selected for indication.

☐ Atrial fibrillation/flutter (AF)

☐ Acute venous thromboembolism (VTE), or prevention of recurrent venous thromboembolism

☐ Primary prophylaxis of VTE in patients undergoing hip or knee replacement surgery^2

☐ Other indication for anticoagulation: local adjudication required^3

Additional Inclusion Criteria

ALL of the following must be fulfilled in order to meet criteria.

☐ Assessment of renal function (CrCl) and hemoglobin, hematocrit, and platelets^4

☐ Provider has assessed DOAC choice, dose, and duration considering the patient's age, renal function, liver function, concurrent medications, and indication for use^5

☐ Modifiable risk factors for bleeding have been identified and addressed, including the concurrent use of drugs that increase major bleed risk (e.g., NSAIDs, antiplatelet therapy)

1. Use caution in Child-Pugh B. Prescribing information varies; rivaroxaban and edoxaban are not recommended. Patients with liver function test elevations greater than 2 to 3 times the upper limit of normal were excluded from clinical trials.
2. Finite duration ranging from about 10 to 35 days. Apixaban, rivaroxaban, or dabigatran are indicated. Dabigatran is approved in hip replacement surgery only. Edoxaban is not FDA approved in this setting.
3. There are separate PBM Criteria for LOW DOSE Rivaroxaban 2.5 mg indicated for reduction of cardiovascular events in patients with peripheral artery disease (PAD) and coronary artery disease (CAD).
4. May also consider liver function testing in patients with a history of or risk for hepatic insufficiency.
5. It is recommended to document the plan for treatment including duration in the patient's chart.

Supplemental Information:

- **For patients with a bioprosthetic heart valve placement in the past 3 months:** A DOAC has been deemed appropriate based on a shared decision-making process between provider and patient given the limited data to support efficacy and safety in this population.
- **Severe renal impairment and/or hemodialysis**: The net clinical benefit of any anticoagulation (warfarin or DOAC) in patients with atrial fibrillation or VTE and severe renal impairment (e.g., CrCl less than 25-30 ml/min) is not well established. An individual evaluation of risks and benefits is recommended, with modifiable risk factors being addressed (e.g., antiplatelet therapy, NSAIDs, etc.). Additional considerations:
  - For dabigatran in patients with CrCl less than 50 ml/min and declining or fluctuating renal function, consider switching to a non-dabigatran DOAC due to the primary renal clearance of dabigatran. When CrCl is less than 30 ml/min, apixaban may be the preferred DOAC.
  - For edoxaban and rivaroxaban in patients with CrCl less than 30 ml/min, apixaban may be the preferred DOAC.
  - For patients with a CrCl <15 ml/min or who are on dialysis, risk of bleeding and thrombotic outcomes is especially high, and the net benefit of anticoagulation (atrial fibrillation) or extended anticoagulation (VTE) is unclear.
- **For edoxaban in atrial fibrillation:** Do not use in patients with CrCl **greater than** 95 ml/min due to reduced efficacy.
- **For patients who can become pregnant:** provide counseling on potential risks vs benefits of treatment and the use of effective contraception during therapy.
- **Appropriate drug dosing:** Drug dosing errors and drug-drug interactions are a significant source of adverse events related to DOACs and should be a priority for review, especially with new starts.
- **Lead-in dosing for acute VTE:**
  - For dabigatran or edoxaban: Patient will/has receive(d) an initial 5 to 10 days of therapy with an injectable anticoagulant (e.g., enoxaparin) BEFORE starting dabigatran or edoxaban
  - For rivaroxaban or apixaban: Patient will/has receive(d) the appropriate oral loading dose of rivaroxaban (15 mg twice daily for 21 days) or apixaban (10 mg twice daily for 7 days) BEFORE starting rivaroxaban or apixaban maintenance doses.

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