Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

Safe initiation of DOAC for patients with CAD/PAD already on guideline directed therapy

ACTION

Administration

DOCUMENT PURPOSE

This order set may be used for patients diagnosed with stable coronary artery disease (CAD) and/or peripheral artery disease (PAD) who are already being treated with guideline directed antiplatelet therapy and require prescription of adjunct direct oral anticoagulant therapy (currently only rivaroxaban) in an inpatient or outpatient setting.

Rivaroxaban is indicated, in combination with aspirin, to reduce the risk of major cardiovascular events (cardiovascular [CV] death, myocardial infarction [MI], and stroke) in patients with chronic CAD or PAD [1].

Other FDA approved pharmacological therapies for cardiovascular prevention can include [1,2,3]:

- Beta blockers
- Blood pressure lowering medication
- Glucose lowering medication
- LDL cholesterol lowering medication
  - Statins
  - PCSK9 inhibitors
  - Other lipid lowering therapies
- Renin angiotensin blockers (ACE-I/ARB)
- Antithrombotic therapies

Note: Specific use of these medications are not addressed in this order set

Eligibility

INCLUSION CRITERIA

Patients should have the following to be eligible for rivaroxaban + aspirin as a secondary prevention strategy [1]:

CORONARY ARTERY DISEASE (CAD) INDICATIONS (SELECT AT LEAST 1 INDICATION AND 1 HIGH-RISK FEATURE)

(1) DOCUMENTED CAD

- ☐ Prior myocardial infarction, or
- ☐ Documented multi-vessel coronary disease (by angiography, stress testing, or coronary revascularization) with a history of stable or unstable angina, or
- ☐ Multi-vessel percutaneous coronary intervention (PCI), or Multi-vessel coronary artery bypass graft (CABG) surgery
- ☐ Multi-vessel coronary artery bypass graft (CABG) surgery

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Eligibility Continued…

INCLUSION CRITERIA CONTINUED…

(2) HIGH-RISK FEATURES

Subjects with CAD must also meet at least one of the following criteria:

- ☐ Age ≥65, or
- ☐ Age <65 and other high-risk features
- ☐ Documented atherosclerosis or revascularization involving at least 2 vascular beds, OR
- ☐ At least 2 additional risk factors:
  - ☐ Current or recent smoker (quit within 1 year) Diabetes mellitus
  - ☐ Renal dysfunction with estimated glomerular filtration rate <60 ml/min
  - ☐ History of symptomatic heart failure
  - ☐ Non-lacunar ischemic stroke ≥1 month ago

AND/OR

PERIPHERAL ARTERY DISEASE (PAD) (SELECT AT LEAST 1)

- ☐ Current or previous PAD revascularization (e.g. aorto-femoral bypass surgery, limb bypass surgery, or percutaneous transluminal angioplasty revascularization of the iliac, or infra-inguinal arteries), or Previous limb or foot amputation for arterial vascular disease, or
- ☐ History of intermittent claudication and one or more of the following: An ankle-brachial index (ABI) < 0.90, or
- ☐ Significant peripheral artery stenosis (≥50%) documented by angiography, or by duplex ultrasound, or
- ☐ Significant carotid artery disease (previous carotid revascularization or asymptomatic carotid artery stenosis ≥50%).

Note: Patients with severe heart failure (ejection fraction <30% or New York Heart Association class III or IV) were not included in the COMPASS randomized trial.

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Eligibility Continued…

USE NOT RECOMMENDED

The following criteria indicate scenarios where rivaroxaban + aspirin should **NOT** be used as a secondary cardiovascular prevention strategy [1]:

- ☐ Active pathological bleeding
- ☐ Advanced chronic kidney disease (estimated CrCl <15 ml per minute)
- ☐ Mechanical heart valves
- ☐ Other indication for anticoagulation (e.g. atrial fibrillation or venous thromboembolism) or antiplatelet medication (e.g. cilostazol)
- ☐ Pregnancy/breastfeeding]
- ☐ Severe hypersensitivity reaction to rivaroxaban or aspirin (e.g. anaphylactic reactions)
- ☐ Any stroke within 1 month
- ☐ Systemic treatment with strong inhibitors of both CYP 3A4 and p-glycoprotein or strong inducers of CYP 3A4
- ☐ Need for aspiring dose >100mg daily
- ☐ Acute limb ischemia within last 2 weeks

USE WITH CAUTION

The following criteria indicate scenarios where use of rivaroxaban + aspirin should be done after carefully considering risks and benefits:

- ☐ Any history of pathologic bleeding
- ☐ High risk of pathologic bleeding
- ☐ History of hemorrhagic or lacunar stroke (>1 month)

Reassess candidacy for anticoagulant prophylaxis as clinically indicated or with any medication changes.

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Factors Influencing Drug Selection

Renal and liver characteristics are necessary to determine appropriateness of anticoagulation therapy.

RENAL FUNCTION

☐ Calculate estimated CrCl using the Cockcroft-Gault formula based on the following:

$$\frac{[(140 - \text{Age}) \times \text{actual weight in kg}]}{[72 \times \text{serum creatinine}]} \times 0.85 \text{ if female}$$

Age: _____

Actual body weight: _____(kg)

Gender: _____

Serum creatinine: _____(mg/dL)

Estimated CrCl: _____ (mL/minute)

RENAL IMPAIRMENT

☐ **AVOID** use in patients with an estimated CrCl <15 ml/min

LIVER FUNCTION

Liver disease: ○ No ○ Yes: Child Pugh Grade: _____

CHILD PUGH SCORE

Measure	1 point	2 points	3 points
Total bilirubin (mg/dL)	< 2	2 - 3	> 3
Serum albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
INR	Less than 1.7	1.7 – 2.2	Greater than 2.2
Ascites	None	Mild (or suppressed with medication)	Moderate to Severe (or refractory)
Hepatic encephalopathy	None	Grade I-II	Grade III-IV

Note: The score employs five clinical measures of liver disease [4] Each measure is scored 1-3, with 3 indicating the worst condition.
Total score of 5-6: grade A (well-compensated disease)
Total score of 7-9: grade B (significant functional compromise)
Total score 10-15: grade C (decompensated disease)

HEPATIC IMPAIRMENT

☐ Child-Pugh A: No adjustment needed

☐ Child-Pugh B/C: **AVOID** use per package insert

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DOAC Drug Interactions and Dose Adjustments

BODY WEIGHT

☐ Underweight *(Weight <50 kg)*: use with caution

CONCOMITANT MEDICATION [1,5]

PHARMACODYNAMIC DRUG INTERACTIONS

- **AVOID** or minimize concomitant use of antiplatelets (*e.g. prolonged dual antiplatelet therapy [DAPT]*), and/or NSAIDs whenever possible
- **AVOID** aspirin doses >100mg daily
- **AVOID** or minimize concomitant use of other forms of aspirin (e.g. Excedrin, Alka-Seltzer, acetylsalicylic acid [ASA])
- **AVOID** or minimize concomitant use of other drugs that impair hemostasis (*e.g. enoxaparin, warfarin, fibrinolytic therapy, SSRIs, SNRIs)* to reduce the risk of bleeding

Orders

☐ Rivaroxaban 2.5 mg PO twice daily

AND

☐ Aspirin 81 mg PO once daily

Be sure to discontinue any P2Y12 antiplatelet therapy when initiating rivaroxaban + aspirin therapy unless immediate post-intervention for PAD. In this case, recommend P2Y12 therapy for ≤30 days

Lab Orders

BASELINE LAB ORDERS (IF NOT CHECKED RECENTLY)

☐ Baseline CBC

☐ Baseline serum creatinine (to calculate Cockcroft Gault formula) Baseline INR (to calculate Child Pugh score)

☐ Baseline liver function tests (to calculate Child Pugh score)

☐ Other (specify): _____

FOLLOW-UP LAB ORDERS

☐ Periodic renal function (e.g., serum creatinine, CrCl) as clinically necessary

☐ Anticoagulant clinic referral as per policy [1,5] s

☐ Other (specify):_____

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Other Considerations

PROTON PUMP INHIBITORS (PPIS)

Note: Clinician may consider PPI or other form of gastroprotection for patients at high risk of GI bleeding, particularly if using multiple antithrombotic agents or with a prior history of upper GI bleeding [6, 7, 8].

MANAGED CARE

- ☐ Complete prior authorization paperwork if required by payer (https://www.covermymeds.com)

SHARED DECISION-MAKING DISCUSSION

Note: If drug costs are a barrier to filling prescriptions for medication, refer patient to appropriate resources.

Select all that have been discussed with patient:

- ☐ Bleeding risk/reversal agents
- ☐ Dosing regimen options (e.g. once vs. twice daily)
- ☐ Lifestyle factors of drug (e.g. diet, blood draws, activities)
- ☐ Out-of-pocket medication cost discussed with patient
- ☐ Other (specify):_____

Patient Education

Provide applicable education materials/instructions to the patient as per policy/procedure [1, 6].

The following topics are important to include within patient education:

- ☐ Follow-up appointments for blood work
  - Follow-up contact information:_____
- ☐ Safety net phone number to call if any barriers or issues after discharge: _____
- ☐ Medication management, including starting/stopping new medication, missed doses and dose change (dose de-escalation or switch to oral therapy at appropriate date/time)
- ☐ Importance of medication adherence
- ☐ Expected duration of anticoagulation therapy
- ☐ Drug/diet considerations (if any)
- ☐ Bleeding and bruising risks
- ☐ When to seek medical attention (e.g. warning signs for bleeding, symptoms of VTE)
- ☐ Written education materials for patient/family/caregivers to review after discharge
- ☐ Medication reconciliation completed
- ☐ Patient education documented per health system policy

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Anticoagulation FORUM

PATIENT INFORMATION

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Additional Orders

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