AdvancedHealth
Bridging the Future of Healthcare

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Direct Oral Anticoagulants Drug Use Criteria

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Includes:

Xarelto©	*Rivaroxaban*
Pradaxa©	*Dabigatran*
Eliquis©	*Apixaban*
Savaysa©	*Edoxaban*

This drug use criteria will be used to determine ongoing coverage of the direct oral anticoagulants following the initial six months of therapy allowed through the Advanced Health formulary.

Guideline for Use:

1. Does the member have an OHP funded condition?
    a. If yes, continue to question 2.
    b. If no, deny as BTL.

2. Does the member have a diagnosis for any of the recommended FDA approved indications (DVT or PE treatment, secondary prevention of recurrent DVT or PE, prophylaxis of DVT in knee or hip replacement surgery, or prevention of stroke or systemic embolism in nonvalvular atrial fibrillation), AND is the appropriate dose of medication being prescribed consistent with the FDA approved prescribing information?
    a. If yes, continue to question 3
    b. If no, deny as not meeting criteria. Use of medications for off label indications is considered experimental and not a covered benefit on OHP.

    ***Note to reviewer: Please coordinate with prescriber prior to denying authorization request for inappropriate dosing to change to FDA approved dosing regimen.*

Indications and Dosing

	Xarelto©	Pradaxa©	Eliquis©	Savaysa©
Deep vein thrombosis	15 mg twice daily for 21 days	150 mg twice daily following	10 mg twice daily for 7 days	60 mg once daily following at

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(DVT) or pulmonary embolism (PE) treatment	followed by 20 mg once daily	at least 5 days of parenteral anticoagulation	followed by 5 mg twice daily	least 5 days of parenteral anticoagulation
Reduction in risk of recurrent DVT/PE	10 mg once daily after initial 6 months of therapy	150 mg twice daily	2.5 mg twice daily after initial 6 months of therapy	**Not indicated**
Nonvalvular atrial fibrillation	20 mg once daily	150 mg twice daily	5 mg twice daily	60 mg once daily
Postoperative DVT prophylaxis (hip and knee replacement surgery)	10 mg once daily • Knee: 12 days • Hip: 35 days	110 mg on day 1 then 220 mg once daily (hip replacement only) • Minimum:10 days • Maximum: 35 days (knee replacement: 10-14 days)	2.5 mg twice daily • Knee: 10-14 days • Hip: 30-35 days	**Not indicated**
Prophylaxis of VTE in acutely ill patients (not at high risk of bleeding)	10mg once daily • Total recommended duration of 31 to 39 days			
Peripheral artery disease, stable or Coronary artery disease, stable	2.5 mg twice daily in combination with 75-100 mg aspirin daily			

Duration of therapy

Provoked DVT/PE • Surgery • Nonsurgical transient risk factors: estrogen therapy, pregnancy, leg injury, flight >8h	• 3 months
Unprovoked DVT/PE	• Low to moderate bleeding risk: extended anticoagulation therapy (no stop date) • High bleeding risk: 3 months

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VTE associated with cancer: LMWH is the preferred agent over VKA, Pradaxa, Xarelto, Eliquis, or Savaysa	• Extended anticoagulation therapy (no stop date)

3. Does the member have any conditions in which the DOACs are not recommended or contraindicated? See chart below.
    a. If yes, deny as not meeting criteria. Warfarin or LMWH are alternatives
    b. If no, approve for appropriate duration of therapy for FDA approved indication medication is prescribed to treat.

	Xarelto©	Pradaxa©	Eliquis©	Savaysa©
Contraindication	-Active bleeding	-Active bleeding -Mechanical prosthetic heart valve	-Active bleeding	-Active bleeding
Use not recommended	-Prosthetic heart valves -Severe renal impairment (CrCl <15 ml/min) -Hepatic impairment (Child-Pugh B and C) -Hepatic disease associated with coagulopathy -Pregnancy -Nursing mothers -Prosthetic heart valves -Triple positive antiphospholipid syndrome - GI/Bariatric surgery (decreased absorption)	-Bioprosthetic heart valve -Severe renal impairment (CrCl <15 ml/min) -Pregnancy -Nursing mothers -Triple positive antiphospholipid syndrome - GI/Bariatric surgery (decreased absorption)	-Age <18 years old -Prosthetic heart valve -Nursing mothers -Pregnancy -Severe hepatic impairment (Child-Pugh C) -Severe renal impairment (CrCl <15 ml/min) -Triple positive antiphospholipid syndrome - GI/Bariatric surgery (decreased absorption)	-Age <18 years old -Mechanical heart valve -Moderate to severe mitral stenosis -CrCl >95 ml/min (nonvalvular atrial fibrillation) -Nursing mothers -Moderate to severe hepatic impairment (Child-Pugh B and C) -Triple positive antiphospholipid syndrome - GI/Bariatric surgery (decreased absorption)
Drug-Drug Interactions	-Anticoagulants -Combined P-gp and strong	-Anticoagulants -Rifampin -P-gp inducers	-Anticoagulants -Combined strong CYP3A4	-Anticoagulants -Rifampin

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	CYP3A4 inhibitors and inducers		and P-gp inhibitors and inducers	

*Example of potential drug-drug interactions:

-Strong CYP3A4 and P-gp Inducers: carbamazepine, phenytoin, rifampin, St. John's wort

-Strong CYP3A4 and P-gp Inhibitors: cobicistat, conivaptan, danoprevir/ritonavir, elvitegravir/ritonavir, ketoconazole, clarithromycin, diltiazem, quinidine, tacrolimus, grapefruit juice

*Note: The International society on Thrombosis and Haemostatis (ISTH) 2016 guideline suggests avoiding the use of DOACs in patients with BMI >40 kg/m2 or weight >120 kg due to lack of clinical data in this population. If used in patients with BMI >40 kg/m2 or weight >120 kg, ISTH suggests measuring peak and trough levels using an anti-factor Xa assay or mass spectrometry. If drug level is below expected range, ISTH recommends changing to Vitamin K antagonist. Advanced Health will not restrict access to DOAC medication based on BMI or weight, however, a note will be sent to the requesting provider alerting them to the lack of clinical data in this population.

Rationale:

Due to high cost of therapy and potential for serious adverse events, drug use criteria help to promote safe, evidence-based prescribing of the direct oral anticoagulants.

FDA Approved Indications:

Xarelto© (rivaroxaban) is FDA indicated for the treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), reduction in the risk of recurrence of DVT and PE, reduction of risk of stroke and systemic embolism in patient with nonvalvular atrial fibrillation, and prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery for prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients, and to reduce the risk of major cardiovascular events in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD).

Savaysa© (edoxaban) if FDA indicated for reduction of risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation and the treatment of DVT and PE following 5-10 days of initial therapy with a parenteral anticoagulant.

Pradaxa© (dabigatran) is FDA indicated in adults for the reduction of risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation, treatment of DVT and PE following 5-10 days of initial therapy with a parenteral anticoagulant, reduction in the risk of recurrence of DVT and PE, and DVT and PE prophylaxis in patients that have undergone hip replacement surgery. Pradaxa© is FDA indicated in pediatric patients 8 to less than 18 years of age for the treatment of venous thromboembolic events who have been treated with a parenteral anticoagulant for at least 5 days and to reduce the risk of recurrence of VTE.

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Eliquis© (apixaban) is FDA indicated for reduction of risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation, prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery, treatment of DVT and PE, and reduction in the risk of recurrent DVT and PE.

References:

1. Xarelto© Prescribing Information. Last updated 8/2021
2. Savaysa© Prescribing Information. Last updated 9/2016
3. Pradaxa© Prescribing Information. Last updated 6/2021
4. Eliquis© Prescribing Information. Last updates 7/2016
5. Kearin C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. CHEST 2016; 149(2):315-352
6. International Society on Thrombosis Haemostasis (ISTH) 2016 Guideline