AdvancedHealth
Bridging the Future of Healthcare

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Direct Oral Anticoagulants

Includes:

Xarelto (rivaroxaban)
Pradaxa (dabigatran)
Eliquis (apixaban)
Savaysa (edoxaban)

Created 10/2016

This drug use criteria will be used to determine ongoing coverage of the direct oral anticoagulants following the initial three 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 (DVT) or pulmonary embolism (PE) treatment	15 mg twice daily for 21 days followed by 20 mg once daily	150 mg twice daily following 5-10 days of parenteral anticoagulation	10 mg twice daily for 7 days followed by 5 mg twice daily	60 mg once daily following 5-10 days of parenteral anticoagulation
Reduction in risk of recurrent DVT/PE	20 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 • Minimum: 10 days • Maximum: 35 days	110 mg on day 1 then 220 mg once daily (hip replacement only) • Minimum:10 days	2.5 mg twice daily • Knee: 12 days • Hip: 35 days	**Not indicated**

Approved by Advanced Health Pharmacy and Therapeutics Committee on 10/28/16.

		• Maximum: 35 days **Not indicated for knee replacement**		

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
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	-Age <18 year old -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	-Age <18 years old -Bioprosthetic heart valve -Severe renal impairment (CrCl <15 ml/min) -Pregnancy -Nursing mothers	-Age <18 years old -Prosthetic heart valve -Nursing mothers -Pregnancy -Severe hepatic impairment (Child-Pugh C) -Severe renal impairment (CrCl <15 ml/min)	-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)
Drug-Drug Interactions	-Anticoagulants -Combined P-gp and strong CYP3A4 inhibitors and inducers	-Anticoagulants -Rifampin	-Anticoagulants -Combined strong CYP3A4 and P-gp inhibitors and inducers	-Anticoagulants -Rifampin

*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

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Dosing Adjustments

	Xarelto	Pradaxa	Eliquis	Savaysa

DVT or PE treatment				30 mg once daily (CrCl 15 to 50 ml/min or body weight ≤60 kg)
Reduction in risk of recurrent DVT/PE	15 mg once daily (CrCl 15 to 50 ml/min)			
Nonvalvular atrial fibrillation	15 mg once daily (CrCl 15 to 50 ml/min)	75 mg twice daily (CrCL 15-30 ml/min)	2.5 mg twice daily (2 or more of the following: age ≥80, weight ≤60 kg, or serum creatinine ≥1.5 mg/dl)	30 mg once daily (CrCl 15 to 50 ml/min)

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.

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 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.

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 8/2016
2. Savaysa Prescribing Information. Last updated 9/2016
3. Pradaxa Prescribing Information. Last updated 11/2015
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