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ridging the Future of Healthcare

Direct Oral Anticoagulants Drug Use Criteria

Created: October 2016 Reviewed: 4/22/19

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 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 guestion 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.

Indications and Dosing

	Xarelto©	Pradaxa©	Eliquis©	Savaysa©
Deep vein	15 mg twice	150 mg twice	10 mg twice	60 mg once daily
thrombosis	daily for 21 days	daily following	daily for 7 days	following 5-10
(DVT) or	followed by 20	5-10 days of	followed by 5	days of
pulmonary	mg once daily	parenteral	mg twice daily	parenteral
		anticoagulation		anticoagulation

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



embolism (PE) treatment				
Reduction in risk	20 mg once daily	150 mg twice	2.5 mg twice	Not indicated
of recurrent DVT/PE	after initial 6 months of	daily	daily after initial 6 months of	
DVI/IL	therapy		therapy	
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 dailyMinimum: 10 daysMaximum: 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
		Maximum: 35 days Not indicated		
		for knee		
		replacement		

Duration of therapy

Duration of therapy	
Provoked DVT/PE	• 3 months
Surgery	
 Nonsurgical transient risk factors: estrogen 	
therapy, pregnancy, leg injury, flight >8h	
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	Extended anticoagulation therapy (no stop
preferred agent over VKA, Pradaxa, Xarelto,	date)
Eliquis, or Savaysa	

- 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	-Active bleeding	-Active bleeding



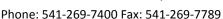
		-Mechanical prosthetic heart valve		
Use not recommended	-Age <18-year- old -Prosthetic heart valves -Severe renal impairment (CrCl <15 ml/min) -Hepatic impairment (Child-Pugh B and C) -Hepatic disease associated with coagulopathy -Pregnancy -Nursing	-Age <18 years old -Bioprosthetic heart valve -Severe 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

^{*}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.





Dosing Adjustments

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

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.

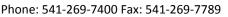
FDA Approved Indications:

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
- 6. International Society on Thrombosis Haemostasis (ISTH) 2016 Guideline