Direct Oral Anticoagulation (DOAC) Follow-up Checklist

PATIENT INFORMATION		
PATIENT NAME:	**DATE:**	**DOSING TIME(S):**
AGE:	**DOAC:**	**WEIGHT:**
	DOSE:	**CHADS$_2$:**

HEALTH STATUS SINCE LAST ASSESSMENT	
Any new relevant medical problems, ED visits/hospitalizations?	☐ Y ☐ N
Any embolic events (stroke / TIA / systemic embolism)?	☐ Y ☐ N
A. ADHERENCE WITH DOAC THERAPY	**ISSUES?** ☐ Y ☐ N
1 or more missed doses in an average week? If yes, number of missed doses:	
Any issues with taking the DOAC properly? *(i.e. rivaroxaban with food/don't open or chew dabigatran/etc.)*	
B. BLEEDING RISK ASSESSMENT *NB: a YES to any of the following requires individualized assessment and does not imply that DOAC should be discontinued*	**ISSUES?** ☐ Y ☐ N
Any signs / symptoms of GI bleeding? Any other bleeding?	
Any drop in hemoglobin or new anemia? Latest hemoglobin:	
EtOH overuse (more than 7 alcoholic drinks per week) ?	
Uncontrolled hypertension (SBP >160 mmHg)? Hypotension with syncope/falls?	
C. CREATININE CLEARANCE	**ISSUES?** ☐ Y ☐ N
Latest creatinine: Latest eGFR (or calculated creatinine clearance if eGFR <50ml/min): http://thrombosiscanada.ca/?page_id=502&calc=cockcroft	
Any recent dehydrating illness or medications added/changed? (i.e. diuretics)	
D. DRUG INTERACTIONS	**ISSUES?** ☐ Y ☐ N
ASA / other antiplatelets? NSAID?	
Other drug interactions? *(Review med list / OTCs; see Table)*	
E. EXAMINATION	**ISSUES?** ☐ Y ☐ N
Blood pressure: ☐ Within Target ☐ High ☐ Low Actual BP (Opt.): /	
Does patient need referral for gait assessment/walking aids for falls prevention?	
F. FINAL ASSESSMENT & RECOMMENDATIONS	
Overall patient appears stable from the anticoagulant standpoint; benefits of continued anticoagulant therapy outweigh risks; Recommend continue current anticoagulant therapy.	☐ Y ☐ N
Dose verified and is appropriate for patient's age/weight/renal function/health status http://thrombosiscanada.ca/?page_id=502&calc=antithromboticAlgorithm	☐ Y ☐ N
Any changes to current therapy needed?	☐ Y ☐ N
Provide details:	

PATIENT EDUCATION & COUNSELING	*I have counselled about the following:*
The rationale for continued DOAC therapy	☐ Y ☐ N
The potential for minor, major or life-threatening bleeding	☐ Y ☐ N
Dosing instructions, adherence, risks of non-adherence, handling missed doses	☐ Y ☐ N
Avoiding OTC ASA & NSAIDs & minimizing EtOH to reduce bleeding risks	☐ Y ☐ N

Next F/U Date	
Next Bloodwork	
Initials	

COMMENTS

Updated:January 15, 2020

This checklist was developed by Gladstone DJ, Geerts WH, Douketis J, Ivers N, Healey JS, Leblanc K. and is a supplement to Ann Int Med. 2015;163:382-386

INDICATION	DOSING OF DIRECT ORAL ANTICOAGULANTS (DOACs)		*Adapted from the AFIB Innovation Program (www.afibinnovationprogram.com)*
	Oral Anticoagulant	**Usual Dose**	**Adjusted Dose**
ATRIAL FIBRILLATION	**Apixaban Eliquis®** (Direct Factor Xa Inhibitor)	5 mg BID	2.5 mg BID Recommended in patients with 2 of the following: age ≥ 80 yrs, body weight ≤ 60 kg, or serum creatinine ≥ 133 µmol/L No dose recommendation can be made if CrCl between 15 and 24 mL/min Avoid in patients with CrCl less than 15 mL/min
	Dabigatran Pradaxa® (Direct Thrombin [IIa] inhibitor)	150 mg BID	110 mg BID Recommended in patients age ≥ 80 yrs or those age ≥ 75 yrs with at least one other bleeding risk factor (i.e. CrCl 30–50 mL/min, concomitant ASA/NSAID, interacting drug, blood dyscrasia, recent bleed etc.) Avoid in patients with CrCl less than 30 mL/min
	Edoxaban Lixiana® (Direct Factor Xa inhibitor)	60 mg daily	30 mg daily Recommended in patients with 1 or more of the following: CrCl 30–50 mL/min, body weight 60 kg or less, or concomitant use of P-gp inhibitors EXCEPT amiodarone and verapamil Avoid in patients with CrCl less than 30 mL/min
	Rivaroxaban Xarelto® (Direct Factor Xa inhibitor)	20 mg daily	15 mg daily Recommended in patients with moderate renal impairment (CrCl 15–49 mL/min) or in combination with a P2Y12 inhibitor in patients who undergo angioplasty with stent placement (max 12 months) Avoid in patients with CrCl less than 15 mL/min. Use with caution if CrCl 15-29 mL/min
VENOUS THROMBO-EMBOLISM	**Apixaban Eliquis®** (Direct Factor Xa Inhibitor)	10 mg BID x 7 days, then 5 mg BID x 3 months minimum 2.5 mg bid may be used for prevention of recurrent VTE after at least 6 months of standard treatment	No dose adjustment if CrCl 30 mL/min or more; use with caution if CrCl between 15 and 29 mL/min; avoid if CrCl less than 15 mL/min
	Dabigatran Pradaxa® (Direct Thrombin [IIa] inhibitor)	Parenteral treatment x 5–10 days, then 150 mg BID x 3 months minimum	110 mg BID Recommended in patients age ≥ 80 yrs or those age ≥ 75 yrs with at least one other bleeding risk factor. Avoid in patients with CrCl less than 15 mL/min; use with caution if CrCl 15–29 mL/min
	Edoxaban Lixiana® (Direct Factor Xa inhibitor)	Parenteral treatment x 5–10 days, then 60 mg daily x 3 months minimum	30 mg daily Recommended in patients with 1 or more of the following: CrCl 30–50 mL/min, body weight 60 kg or less, or concomitant use of P-gp inhibitors EXCEPT amiodarone and verapamil Avoid in patients with CrCl less than 30 mL/min
	Rivaroxaban Xarelto® (Direct Factor Xa inhibitor)	15 mg BID x 21 days, then 20 mg daily x 3 months minimum 10 mg OR 20 mg daily may be used for prevention of recurrent VTE after at least 6 months of standard treatment	No dose adjustment if CrCl 15 mL/min or more; use with caution if CrCl 15–29 mL/min; avoid if CrCl less than 15 mL/min

ADMINISTRATION INFORMATION	*1.Song Y, et al. Clinical Pharmacology and Therapeutics. 2003;93(Suppl 1):S120-1; 2.Moore KT, et al. Clinical Pharmacology in Drug Development. 2004;3(4):321-7*
Apixaban Eliquis®	• May be taken twice daily without regard to meals/food • For NG Administration, may be crushed and suspended in 60 mL water[1]
Dabigatran Pradaxa®	• Must not crush, chew or open capsules (increases exposure by almost double (1.8 times)) • Must be stored in original packaging (foil or bulk bottle) as light, moisture can cause product breakdown
Edoxaban Lixiana®	• May be taken once daily without regard to meals/food
Rivaroxaban Xarelto®	• Doses of 15–20 mg must be taken with food (AUC increases 39%, Cmax increases 75% with food) • For NG Administration, may be crushed and suspended in 50 mL water; follow immediately with food (enteral feeds); ensure NG tube not distal to stomach or decreased absorption can occur[2]

DRUG INTERACTIONS THAT MAY AFFECT DOAC DRUG LEVELS

Potential ↑ in Apixaban		Potential ↓ in Apixaban	Potential ↑ in Dabigatran		Potential ↓ in Dabigatran	
*Diltiazem**	*Naproxen**	*Carbamazepine¥*	*Amiodarone**	*Quinidine*§*	*Antacids§*	*Strong P-glycoprotein inducers‡*
Ketoconazole, itraconazole, voriconazole, posaconazole = azole-antimycotics‡	*Ritonavir (all HIV protease inhibitors)‡*	*Phenobarbital¥*	*Clarithromycin**	*Ritonavir**	*Atorvastatin***	
	Strong inhibitors of both P-glycoprotein and CYP 3A4‡	*Phenytoin¥*	*Cyclosporine**	*Saquinavir**	*Carbamazepine¥*	
		Rifampin¥	*Dronedarone¥*	*Tacrolimus**	*Proton Pump Inhibitors**	
		St. John's Wort¥	*Itraconazole**	*Tipranavir¥*	*Rifampin¥*	
		Strong inducers of both P-glycoprotein and CYP-3A4¥	*Ketoconazole‡*	*Ticagrelor¥*	*St. John's Wort¥*	
			*Nelfinavir**	*Verapamil*§*	*Tenofovir¥*	
			*Posaconazole**	*Strong P-glycoprotein inhibitors‡*		

Potential ↑ in Edoxaban		Potential ↓ in Edoxaban	Potential ↑ in Rivaroxaban		Potential ↓ in Rivaroxaban	
*Amiodarone**	*Ketoconazole£*	*Atorvastatin**	*Clarithromycin**	*Posaconazole‡*	*Carbamazepine¥*	*Strong inducers of both P-glycoprotein and CYP 3A4¥*
Cyclosporine£	*Quinidine£*	*Carbamazepine¥*	*Erythromycin**	*Ritonavir‡*	*Phenobarbital¥*	
*Digoxin**	*Verapamil**	*Esomeprazole**	*Fluconazole**	*Strong inhibitors of both P-glycoprotein and CYP 3A4‡*	*Phenytoin¥*	
Dronedarone£	*Protease Inhibitors¥*	*Phenobarbital¥*	*Ketoconazole‡*		*Rifampin¥*	
Erythromycin£		*Phenytoin¥*	*Itraconazole‡*		*St. John's Wort¥*	
		Rifampicin¥				

Note that drug interaction data with the DOACs is limited and this table reflects currently available data. Consider Pharmacist consult as needed. Dabigatran etexilate and edoxaban are substrates for the P-glycoprotein transporter (P-gp) and as such any strong inhibitors or inducers should be avoided. Rivaroxaban and apixaban are eliminated by both P-gp and cytochrome P-450 3A4 (CYP-450 3A4). As such the concomitant use of strong inhibitors and inducers of both P-gp and 3A4 should be avoided.

**no empiric dosage adjustment required, however use with caution, § recommend to give 2 hours after dabigatran, ‡contraindicated, ¥ caution advised if co-administering, should be avoided, £ reduce dose of edoxoban to 30 mg daily, **no dose adjustment is required*

PRE-OPERATIVE MANAGEMENT OF PATIENTS RECEIVING DIRECT ORAL ANTICOAGULANTS FOR ATRIAL FIBRILLATION			
Drug (dose regimen)	**Renal Function**	**Minor Surgery/Procedure (Low Bleeding Risk)** 12–15% residual anticoagulant effect at time of surgery acceptable	**Major Surgery/Procedure or Spinal Anesthesia (High Bleeding Risk)** <10% residual anticoagulant effect at time of surgery acceptable
		For examples of low and high risk bleeding procedures visit: http://thrombosiscanada.ca/?page_id=502&calc=perioperativeAnticoagulantAlgorithm	
Apixaban Eliquis® (twice daily)			
$t_{1/2}$ = 9 hours	Normal renal function or mild impairment (CrCl > 30 mL/min)	Last dose: 2 days before surgery (skip 2 doses)	Last dose: 3 days before surgery (skip 4 doses)
Dabigatran Pradaxa® (twice daily)			
$t_{1/2}$ = 14 hours	Normal renal function or mild impairment (CrCl > 50 mL/min)	Last dose: 2 days before surgery (skip 2 doses)	Last dose: 3 days before surgery (skip 4 doses)
$t_{1/2}$ = 15–18 hours	Moderate renal impairment (CrCl 30 – 50 mL/min)	Last dose: 3 days before surgery (skip 4 doses)	Last dose: 4 to 5 days before surgery (skip 6–8 doses)
Edoxaban Lixiana® (once daily)			
$t_{1/2}$ = 10–14 hours	Normal renal function or mild impairment (CrCl ≥ 50 mL/min)	Last dose: 2 days before surgery (skip 1 dose)	Last dose: 3 days before surgery (skip 2 doses)
Rivaroxaban Xarelto® (once daily)			
$t_{1/2}$ = 9 hours	Normal renal function or mild impairment (CrCl > 30 mL/min)	Last dose: 2 days before surgery (skip 1 dose)	Last dose: 3 days before surgery (skip 2 doses)

This table provides general guidance and may not be applicable to all patients including those undergoing neuroaxial anaesthesia. Consultation with a specialist is advised for specific patient management, particularly in patients with an active thrombus such as those with VTE.

Adapted from www.thrombosiscanada.ca/wp-content/uploads/2014/05/Peri-operative-Management-of-Patients-who-are-Receiving-a-New-Oral-Anticoagulant-dabigatran-rivaroxaban-apixaban.pdf

TYPES OF CLINICAL BLEEDING	
Minor bleeding	Self-limited bleeding events. Examples include subconjunctival hemorrhage, small bruising/lacerations, dental bleeding, anterior epistaxis and hemorrhoidal bleeding.
Moderate bleeding	Bleeding events requiring medical attention and actual or potential need for blood transfusion or definitive intervention. Examples include hemodynamically stable gastrointestinal bleeding and uncontrolled posterior epistaxis.
Severe/Life-threatening bleeding	Bleeding events requiring urgent medical attention and causing actual or impending hemodynamic compromise. Examples include intracranial hemorrhage, bleeding into another critical site (e.g. retroperitoneal, intra-spinal, intra-ocular, intra-articular), massive gastrointestinal bleed or other clinically overt bleeding with hemoglobin decrease ≥20 g/L or administration of ≥2 units RBCs

Adapted from: Thrombosis Canada Clinical Guide: New/Novel Oral Anticoagulants (NOACS): Management of Bleeding (2016)