# DIRECT ORAL ANTICOAGULANT (DOAC) FOLLOW-UP CHECKLIST

**Patient name:**

**Age:**

***Date*** _____

***DOAC*** _____

***Dose*** _____

***Dosing Time(s)*** _____

***Weight*** _____

***$CHADS_2$*** _____

**COMMENTS**

| | | | | |
|---|---|---|---|---|
| | **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?** | | | |
| | **Uncontrolled hypertension (SBP >160 mmHg)? Hypotension with syncope/falls?** | | | |
| **C** | **CREATININE CLEARANCE** | **Issues?** | ❒ Y | ❒ N |
| | **Latest creatinine: _____**<br>**Latest eGFR (or calculated creatinine clearance if eGFR <50ml/min): _____**<br>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**<br>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:*** | ❒ Y | ❒ N |
| | **The rationale for continued DOAC therapy** | | | |
| | **The potential for minor, major or life-threatening bleeding** | | | |
| | **Dosing instructions, adherence, risks of non-adherence, handling missed doses** | | | |
| | **Avoiding OTC ASA & NSAIDs & minimizing EtOH to reduce bleeding risks** | | | |

***Next F/U Date*** _____

***Next Bloodwork*** _____

***Initials*** _____

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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) | | |
|---|---|---|---|
| | **Oral Anticoagulant** | **Usual Dose** | **Adjusted Dose** |
| **Atrial Fibrillation** | **Apixaban Eliquis®** (Direct Factor Xa Inhibitor) | 5 mg BID | 2.5 mg BID<br>Recommended in patients with 2 of the following: age ≥ 80 yrs, body weight ≤ 60 kg, or serum creatinine ≥ 133 µmol/L<br>No dose recommendation can be made if CrCL between 15 and 24 mL/min<br>Avoid in patients with CrCl less than 15 mL/min |
| | **Dabigatran Pradaxa®** (Direct Thrombin [IIa] inhibitor) | 150 mg BID | 110 mg BID<br>Recommended in patients age ≥ 80 yrs or those age ≥ 75 yrs with at least one other bleeding risk factor (i.e. CrCl 30-50mL/min, concomitant ASA/NSAID, interacting drug, blood dyscrasia, recent bleed etc.)<br>Avoid in patients with CrCl less than 30 ml/min |
| | **Edoxaban Lixiana®** (Direct Factor Xa inhibitor) | 60 mg daily | 30 mg daily<br>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<br>Avoid in patients with CrCl less than 30 mL/min |
| | **Rivaroxaban Xarelto®** (Direct Factor Xa inhibitor) | 20 mg daily | 15 mg daily<br>Recommended in patients with moderate renal impairment (CrCL 30 - 49 ml/min)<br>Avoid in patients with CrCl less than 30 ml/min |
| **Venous Thromboembolism** | **Apixaban Eliquis®** (Direct Factor Xa Inhibitor) | 10 mg BID x 7 days, then 5 mg BID x 3 months minimum | 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<br>Recommended in patients age ≥ 80 yrs or those age ≥ 75 yrs with at least one other bleeding risk factor.<br>Avoid in patients with CrCl less than 30 ml/min |
| | **Edoxaban Lixiana®** (Direct Factor Xa inhibitor) | 60 mg daily | 30 mg daily<br>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<br>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 | No dose adjustment if CrCl 30 mL/min or more; avoid if CrCl less than 30 mL/min |

*Adapted from the AFIB Innovation Program (www.afibinnovationprogram.com)*

| ADMINISTRATION INFORMATION | |
|---|---|
| **Apixaban Eliquis®** | • May be taken twice daily without regard to meals/food<br>• 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))<br>• 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)<br>• 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] |

*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*

## 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*** | |
| | | *Phenytoin¥* | *Cyclosporine** | *Saquinavir** | *Carbamazepine¥* | |
| | *Strong inhibitors of both P-glycoprotein and CYP 3A4‡* | *Rifampin¥* | *Dronedarone¥* | *Tacrolimus** | *Proton Pump Inhibitors** | *Phenytoin¥* |
| | | *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 30mg 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)<br>12-15% residual anticoagulant effect at time of surgery acceptable | Major Surgery/Procedure or Spinal Anesthesia (High Bleeding Risk)<br><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)*