What are the recommendations for the novel oral anticoagulants (NOACs) (apixaban, dabigatran, rivaroxaban) versus warfarin for patients with nonvalvular atrial fibrillation?

- **Overall:** exact role to be determined due to limited real world experience with the new agents
- **Canadian:** CCS[2012], Thrombosis Canada[2013]: NOACs are **preferred** over warfarin, CADTH[2012]: **1st line=warfarin**; 2nd line=NOACs for patients not doing well on warfarin
- **American:** CHEST[2012]: dabigatran **preferred** over warfarin. AHA/ASA[2012]: NOACs are **alternatives** to warfarin; AAN[2014]: **no preference** - choose one of warfarin, dabigatran, rivaroxaban or apixaban[18]
- European: ESC[2012]: NOACs **preferred** over warfarin, EHRA[2013]: NOACs are **alternatives** to warfarin

Consider warfarin in patients with valvular heart disease, poor renal function, controlled on warfarin & no concerns with INR monitoring, and/or at risk of dyspepsia[dabigatran] or GI bleed.

Considerations	Warfarin Coumadin	Dabigatran Pradaxa	Apixaban Eliquis	Rivaroxaban Xarelto
Mechanism	Vitamin K Inhibitor (Factors II, VII, IX, X & Proteins C, S)	Direct Thrombin Inhibitor	Direct Factor Xa Inhibitor	Direct Factor Xa Inhibitor
Experience	Approximately 60 years	Median follow-up = 2 years[RE-LY,19] Mean $CHADS_2$ score = 2.1, n=18,113	Median follow-up = 1.8 years[ARISTOTLE,20] Mean $CHADS_2$ score = 2.1, n=18,201	Median follow-up = 1.9 years[ROCKET-AF,21] Mean $CHADS_2$ score = 3.5, n=14,264
Efficacy	Reduces the risk of stroke by 65% Depends on the time spent in therapeutic range	150mg bid: Superior to warfarin for stroke or systemic embolism (NNT=88 in 2 years); Hemorrhagic stroke: 0.10%/y vs 0.38%/y warfarin; Ischemic stroke: 0.92%/y vs 1.21%/y warfarin 110mg bid: Non-inferior to warfarin	Superior to warfarin for stroke or systemic embolism (NNT=167) & mortality (NNT=132) Hemorrhagic stroke: 0.24%/y vs 0.47%/y warfarin; Ischemic stroke: 0.97%/y vs 1.51%/y warfarin	Non-inferior to warfarin for stroke or systemic embolism Hemorrhagic stroke: 0.26%/y vs 0.44%/y warfarin; Ischemic stroke: 1.34%/y vs 1.42%/y warfarin
Safety	Risk of nonhemorrhagic stroke when INR < 2 Risk of bleed when INR > 3 Overall rate of hemorrhage in Ontario[22] **Intracranial: 0.2% per person-year** **Upper GI: 1.0% per person-year** **Lower GI: 1.4% per person-year**	150mg bid: no difference in major bleeds, less intracranial bleed (0.32%/y vs 0.76%/y warfarin, NNT=116), more GI bleed (1.56%/y vs 1.07%/y warfarin, NNH=100), more dyspepsia (NNH=18) vs warfarin; Increase MI risk? 110mg bid: less major bleed (NNT=77), less intracranial bleed (0.23%/y vs 0.76%/y warfarin, NNT=96), more dyspepsia (NNH=17) vs warfarin	Less major bleed (NNT=67), less intracranial bleed (0.33%/y vs 0.80%/y warfarin, NNT=128), no difference in GI bleed (0.76%/y vs 0.86%/y warfarin) vs warfarin	No difference in major bleed, less intracranial bleed (0.5%/y vs 0.7%/y warfarin, NNT=250), more GI bleed (3.2% vs 2.2% warfarin, NNH=100), more epistaxis (NNH=67), more hematuria (NNH=125) vs warfarin
Antidote	Vitamin K 1-10mg PO	No established antidote Potential options: dialysis, activated charcoal if < 2-3 h of administration	No established antidote Potential options: prothrombin complex concentrate, recombinant factor VIIa, activated charcoal if < 2-3 h	No established antidote Potential options: prothrombin complex concentrate, recombinant factor VIIa, activated charcoal if < 2-3 h
Monitoring	Routine & frequent INR tests, up to q3months	SCr & calculated CrCl – at least annually	SCr & calculated CrCl – at least annually	SCr & calculated CrCl – at least annually
Drug interactions	Numerous well-documented drug interactions INR monitoring more frequently	Contraindicated: dronedarone, ketoconazole Avoid: rifampicin Caution: P-gp inhibitor↑[dabigatran] (amiodarone, clarithromycin, cyclosporine, itra-, posa-conazole, nelfin- ,riton-, sequin-, tipran-avir, quinidine, tacagrelor, tacrolimus, verapamil[Take dabi 2 hrs before]); P-gp inducer↓[dabigatran] (carbamazepine, St. John's Wort, tenofovir) Antacids ↓[dabigatran] (H_2RA, PPI, Al-Mg Hydroxide)[Take dabigatran 2 hours before antacid]	Contraindicated: keto, itra, posacon-azoles, ritonavir Caution: CYP 3A4 and P-gp inducers (carbamazepine, phenytoin, rifampin, St. John's Wort) and inhibitors (amiodarone, dronedarone, quinidine, verapamil)	Contraindicated: itra, keto, posacon-azoles, ritonavir Caution: CYP 3A4 and P-gp inducers (carbamazepine, clarithromycin, phenytoin, rifampin, St. John's Wort)
Half-life	Longer half-life (2.5 days)	Half-life = 12-17 hours	Half-life = 12 hours	Half-life = 5-9 hrs (young), 11-13 hrs (elderly)
Dosage[CPS]	Once daily, target INR 2-3	150mg po twice daily 110mg po twice daily in patients who are ≥ 80 y or who are 75-79 y with ≥ 1 **bleeding risk factor***	5mg po twice daily 2.5mg po twice daily in patients with ≥ 2 of the following criteria: age ≥ 80, body weight ≤ 60kg, or SCr ≥ 133 umol/L	20mg po once daily CrCl 30-49mL/min: 15mg po once daily
Renal function	No dosage adjustment required	Contraindicated if CrCl < 30mL/min	Excluded patients with CrCl < 25mL/min CrCL < 15mL/min not recommended	CrCl 30-49mL/min: 15mg po daily CrCl < 30mL/min not recommended
Switch TO →	Switch FROM **Apix** or **Rivar** TO → **Warfarin:** Start warfarin, stop **Apix** or **Rivar** when INR > 2 Switch FROM **Dabigatran** TO → **Warfarin:** CrCl>50mL/min: start warf 3 days before D/C **dabi** CrCl 31-50mL/min: start warf 2 days before D/C **dabi** CrCl 15-30mL: start warfarin 1 day before D/C **dabi**	Switch FROM **Warfarin** TO → **Dabigatran** Stop **warfarin**. Start **Dabigatran** when INR<2	Switch FROM **Warfarin** TO → **Apixaban** Stop **warfarin**. Start **Apixaban** when INR < 2	Switch FROM **Warfarin** TO → **Rivaroxaban** Stop **warfarin**. Start **Rivar** when INR < 2
Limited Use[ODB]	None	Code for non-valvular atrial fibrillation: 432	Code for non-valvular atrial fibrillation: 448	Code for non-valvular atrial fibrillation: 435
Cost/month	$40 (includes INR monitoring cost)+dispensing fee	$96+dispensing fee	$96+dispensing fee	$85.20+dispensing fee
Dabigatran Pradaxa issues	*Bleeding Risk Factors: Moderate renal impairment[30-50mL/min], P-gp inhibitor, NSAID, anti-platelets[eg. ASA, clopidogrel], congenital/acquired coagulation disorders, thrombocytopenia or functional platelet defects, active/recent ulcerative GI bleeding, recent biopsy or major trauma, recent intracranial hemorrhage, surgery[brain, spinal or ophthalmic], bacterial endocarditis, age ≥ 75 y; Store capsules in original containers; cannot be in dosette or compliance package			

Limited Use Criteria for non-valvular atrial fibrillation

Apixaban

Code	Clinical Criteria
448	INCLUSION CRITERIA: At risk patients with non-valvular atrial fibrillation, for the prevention of stroke and systemic embolism AND in whom: 1. Anticoagulation is inadequate following at least a 2-month trial on warfarin; OR 2. Anticoagulation using warfarin is contraindicated or not possible due to inability to regularly monitor the patient via International Normalized Ratio (INR) testing (i.e. no access to INR testing services at a laboratory, clinic, pharmacy, and at home) EXCLUSION CRITERIA: 1. Patients with impaired renal function (creatinine clearance or estimated glomerular filtration rate less than 25mL per min); OR 2. Patients who are greater than or equal to 75 years of age and who do not have documented stable renal function; OR 3. Patients who have hemodynamically significant rheumatoid valvular heart disease (especially mitral stenosis); OR 4. Patients who have prosthetic heart valves. NOTES: At-risk patients with atrial fibrillation are defined as those with a CHADS2 score of greater than or equal to 1. Prescribers may consider an antiplatelet regimen or oral anticoagulation for patients with a CHADS2 score of 1. Inadequate anticoagulation is defined as INR testing results that are outside the desired INR range for at least 35% of the tests during the monitoring period (i.e., adequate anticoagulation is defined as INR test results that are within the desired INR range for at least 65% of the tests during the monitoring period). Documented stable renal function is defined as creatinine clearance or estimated glomerular filtration rate maintained for at least 3 months. DOSING: the usual recommended dose is 5mg twice daily; a reduced dose of apixaban 2.5mg twice daily is recommended for patients with at least two (2) of the following: age greater than or equal to 80 years old, body weight less than or equal to 60kg, or serum creatinine greater than or equal to 133 micromole per litre. Since renal impairment can increase bleeding risk, renal function should be regularly monitored. Other factors that increase bleeding risk should also be assessed and monitored (see apixaban product monograph). Patients starting apixaban should have ready access to appropriate medical services to manage a major bleeding event. There is currently no data to support that apixaban provides adequate anticoagulation in patients with rheumatic valvular disease or those with prosthetic heart valves. As a result, apixaban is not recommended for these patient populations. LU Authorization Period: Indefinite

Dabigatran

Code	Clinical Criteria
432	For the prevention of stroke and systemic embolism in at risk patients with non-valvular atrial fibrillation (AF), AND in whom: 1) Anticoagulation is inadequate following a reasonable trial on warfarin; OR 2) Anticoagulation with warfarin is contraindicated or not possible due to inability to regularly monitor via International Normalized Ratio (INR) testing (i.e., no access to INR testing services at a laboratory, clinic, pharmacy, and at home). Exclusion Criteria: Impaired renal function (creatinine clearance or estimated glomerular filtration rate less than 30mL/min); OR greater than or equal to 75 years of age without documented stable renal function; OR hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis; OR prosthetic heart valves. Note: (a) Documented stable renal function is defined as creatinine clearance or estimated glomerular filtration rate maintained for at least 3 months (i.e., 30-49mL/min for 110mg twice daily dosing and, greater than or equal to 50mL/min for 150mg twice daily dosing for at least 3 months). (b) At risk patients with atrial fibrillation are defined as those with a CHADS2 score of greater than or equal to 1. (c) Inadequate anticoagulation is defined as INR testing results that are outside of the desired INR range for at least 35% of the tests during the monitoring period (i.e., adequate anticoagulation is defined as INR test results that are within the desired INR range for at least 65% of the tests during the monitoring period). (d) A reasonable trial on warfarin is defined as at least 2 months of therapy. (e) Since renal impairment can increase bleeding risk, renal function should be regularly monitored. Other factors that increase bleeding risk should also be assessed and monitored (see product monograph). (f) Patients starting dabigatran should have ready access to appropriate medical services to manage a major bleeding event. (g) There are currently no data to support that dabigatran provides adequate anticoagulation in patients with rheumatic valvular disease or those with prosthetic heart valves; dabigatran is not recommended in these populations. LU Authorization Period: Indefinite

Rivaroxaban

Code	Clinical Criteria
435	For the prevention of stroke and systemic embolism in at-risk patients who have non-valvular atrial fibrillation (AF) AND in whom: 1) Anticoagulation is inadequate following a reasonable trial on warfarin; OR 2) Anticoagulation with warfarin is contraindicated or not possible due to inability to regularly monitor via International Normalized Ratio (INR) testing (i.e., no access to INR testing service at a laboratory, clinic, pharmacy, and at home). Exclusion Criteria: Patients who: (a) have impaired renal function (creatinine clearance or estimated glomerular filtration rate less than 30mL/min); OR (b) are greater than or equal to 75 years in age without documented stable renal function; OR (c) have hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis; OR (d) have prosthetic heart valves. Definitions and Clarification: (a) "documented stable renal function" is defined as creatinine clearance or estimated glomerular filtration rate that maintained for at least 3months (i.e., 30-49mL/min for 15mg once daily dosing or greater than or equal to 50mL/min for 20mg once daily dosing for at least 3 months). (b) "at-risk patients with atrial fibrillation" are defined as those with a CHADS2 score of greater than or equal to 1. Although the ROCKET-AF trial included patients with higher CHADS2 score (greater than or equal to 2), other landmark studies with the other newer oral anticoagulants demonstrated a therapeutic benefit in patients with a CHADS2 score of 1. Prescribers may consider an antiplatelet regimen or oral anticoagulation for patients with a CHADS2 score of 1. (c) "inadequate anticoagulation" is defined as INR testing results that are outside of the desired INR range for at least 35% of the tests during the monitoring period (i.e., adequate anticoagulation is defined as INR test results that are within the desired INR range for at least 65% of the tests during the monitoring period). (d) "a reasonable trial on warfarin" is defined as at least 2 months of therapy. (e) Since renal impairment can increase bleeding risk, renal function should be regularly monitored. Other factors that increase bleeding risk should also be assessed and monitored (see Xarelto product monograph). (f) Patients starting rivaroxaban should have ready access to appropriate medical services to manage a major bleeding event. (g) There is currently no data to support that rivaroxaban provides adequate anticoagulation in patients with rheumatic valvular disease or those with prosthetic heart valves, so rivaroxaban is not recommended in these populations. LU Authorization Period: Indefinite

Perioperative Management – Before & After an Invasive Procedure[1,2,3,4]

March 2014

Key Messages

- There is no strong evidence-based indications for bridging anticoagulation[6,7,8,9,10]; bridging has a 3% risk for major bleeding & 10-15% risk of minor bleeding[2]
- The absolute risk of an embolic event for patients in whom anticoagulation is interrupted for 4 to 7 days is approximately 1% within 30 days[11,12]
- Bridging is suggested in **high** thromboembolic (TE) risk patients, not suggested in **low** TE risk patients & optional in **intermediate** TE risk patients[1]
- For patients on **apixaban**, **dabigatran** or **rivaroxaban** (NOACs), "unfractionated heparin (UFH) or low molecular weight heparin (LMWH) bridging" is **NOT** required[3]
- CAUTION: Delaying surgery and holding warfarin (without bridging) for too long will increase risk of stroke[anecdotal case reports] – use clinical judgment!!
- For patients receiving **ASA** and have moderate to high risk of heart disease (e.g. diabetes), continue **ASA** before, during, and after surgery

Recommendations for Antiplatelets & NSAIDS in Perioperative Procedures[1,4,13,14,15,16,17]

	Drug	Stop before surgery
Antiplatelet	ASA[Aspirin]	Depends
	Clopidogrel[Plavix]	5 days (see below)
	Prasugrel[Effient]	7 days (see below)
	Ticagrelor[Brilinta]	5 days (see below)
	Ticlopidine[Ticlid]	14 days
NSAIDS	Celecoxib[Celebrex]	2-3 days
	Ibuprofen[Advil/Motrin]	½ day
	Ketorolac[Toradol]	1 day
	Meloxicam[Mobicox]	3 days
	Naproxen[Aleve]	3 days

CHEST 2012 recommendations

Patients receiving **ASA** and:

- Undergoing a diagnostic test,
  - Associated with a low risk of bleeding (eg. minor dental, dermatologic or cataract surgery), **continue ASA**
  - Associated with a high risk of bleeding, **D/C ASA** 7-10 day prior to surgery
- Undergoing arthrocentesis may **continue ASA**
- Undergoing noncardiac surgery & at low risk of CV events, **stop ASA** 7-10 days before surgery
- In patients at moderate to high risk (eg, ischemic heart disease, compensated or prior heart failure, diabetes, renal insufficiency, or cerebrovascular disease) who are receiving ASA therapy & require noncardiac surgery, suggest **continue ASA**
- Require CABG, **continue ASA**
- **Remind patient to restart ASA after surgery**

Patients receiving **dual antiplatelet therapy (DAPT)**:[Chest 2012]

- Patients with **coronary stent** having surgery
  - Recommend **deferring** (any) **surgery** for at least 6 weeks after a bare-metal stent & for at least 6 months after a drug-eluting stent instead of undertaking surgery
  - In patients who require surgery within 6 weeks of a bare-metal stent or within 6 months of a drug-eluting stent, suggest **continue DAPT** around the time of surgery
- Require CABG surgery, **continue ASA** & **stop clopidogrel[Plavix]/ticagrelor[Brilinta]** 5 days before surgery or **stop prasugrel[Effient]** 7 days before surgery
- POST-OP: In patients with ACS, restart dual antiplatelet therapy at maintenance dose within **48-72 hours** when deemed safe by the cardiac surgical team

Examples

A. *70y male taking **EC ASA 81mg daily** for primary prevention of cardiovascular disease and is scheduled for **2 teeth extractions** next week.*
B. *68y female with Type 2 Diabetes and Osteoporosis taking **Naproxen 375mg tid** for OA of knee and undergoing **right knee replacement**.*
C. *72y female with coronary stent placed 1.5 years ago and taking both **EC ASA 81mg** daily and **clopidogrel 75mg** daily (as per cardiologist) and is undergoing cataract surgery.*
D. *80y male taking **EC ASA 81mg** daily for secondary prevention of cardiovascular disease and is scheduled for **colonoscopy**.*
E. *75y female with AF, hypertension, diabetes, and prior stroke is undergoing **cataract removal** and is taking **warfarin** (INR = 2.3)*
F. *66y male is taking **rivaroxaban Xarelto** 20mg po od for recurrent VTEs (DVT 6 and 12 months ago) and has elective surgery for **transurethral resection of the prostate (TURP)**.*
G. *68y male with AF, heart failure, diabetes, and heart failure is undergoing **colonoscopy** and is taking **warfarin** (INR = 2.8)*

Answers: A. Continue ASA **B.** Stop Naproxen 3 days before right knee replacement **C.** Continue ASA and stop clopidogrel 5 days before surgery **D.** Continue ASA (high risk of ischemic heart disease)		
E. Step 1: Cataract removal = Very Low risk of bleed	**Step 2**: Skip because of very low risk of bleed	**Step 3**: Warfarin = No need to stop before surgery
F. Step 1: TURP = Major urologic surgery = High risk of bleed	**Step 2**: Skip because on NOAC (rivaroxaban)	**Step 3**: Pre-op = skip 2 doses prior, Post-op = resume after 2 days
G. Step 1: Colonoscopy = Low risk, Polypectomy = High risk	**Step 2**: $CHADS_2$ = 4 = High risk of TE → Bridging is optional	**Step 3**: Warfarin = stop 5 days prior (polypectomy?), resume day after

References available upon request

Prepared by Margaret Jin, PharmD & HFHT Pharmacy Program

Perioperative Management – Before & After an Invasive Procedure [1,2,3,4] March 2014

Steps for Managing Perioperative Antithrombotic Therapy [Warfarin[Coumadin] & Novel Oral Anticoagulants (NOACs) {Apixaban[Eliquis], Dabigatran[Pradaxa], Rivaroxaban[Xarelto]}]

Step 1: Determine the procedure bleeding risk[5]	Step 2: Determine the TE risk (to bridge or not to bridge?)	Step 3: Choose pre-op/post-op management accordingly

Very low

Cataract removal, dental extractions (1 or 2 teeth) or teeth cleaning, minor skin procedure (eg. skin biopsy or skin cancer removal)

For **Very Low** procedure bleeding risk (Thrombosis Canada):
Continue anticoagulation (warfarin & NOACs).
It is likely safe to not interrupt anticoagulation, but data to support such a practice is lacking. Thrombosis Canada

Low

For Very Low & Low bleeding risk → go to Step 3

Coronary angiography, Dental/Dermatologic procedures
Endoscopic Procedures [Capsule endoscopy, Diagnostic (colonoscopy, esophagogastroduodenoscopy, flexible sigmoidoscopy) including biopsy, Endoscopic retrograde cholangiopancreatography without sphincterotomy, Endoscopic ultrasonography without fine-needle aspiration, Enteral stent deployment (without dilation), Enteroscopy and diagnostic balloon-assisted enteroscopy]
Laparoscopic cholecystectomy or inguinal hernia repair
Ophthalmologic procedures
Selected invasive procedures [bone marrow aspirate & biopsy, lymph node biopsy, thoracentesis, paracentesis, arthrocentesis]

For **Low** procedure bleeding risk (Thrombosis Canada):

WARFARIN[1,2]	NOACs	
	PRE-OP	POST-OP
No need to stop warfarin before surgery or procedure	**Apixaban** (BID) *(skip 2 doses)* Last dose: 2 days before Sx	**Apixaban** (BID) Resume 1 day after Sx
	Dabigatran (BID) CrCl > 50mL/min *(skip 2 doses)* Last dose: 2 days before Sx CrCl 30-50mL/min *(skip 4 doses)* Last dose: 3 days before Sx	**Dabigatran** (BID) Resume 1 day after Sx
	Rivaroxaban (OD) *(skip 1 dose)* Last dose: 2 days before Sx	**Rivaroxaban** (OD) Resume 1 day after Sx

High

Cardiac surgery [CABG or heart valve replacement]
Endoscopic Procedures [Biliary or pancreatic sphincterotomy, Cystogastrostomy, Endoscopic hemostasis, Endoscopic ultrasonography with fine-needle aspiration, Percutaneous endoscopic gastrostomy placement, Pneumatic or bougie dilation, Polypectomy, Therapeutic balloon-assisted enteroscopy, Treatment of varices, Tumor ablation by any technique]
Intestinal anastomosis surgery
Lung resection surgery
Major lower limb orthopedic surgery [hip/knee joint replacement]
Major urologic surgery [prostatectomy, bladder tumour resection]
Major vascular Surgery [abdominal aortic aneurysm repair, aortofemoral bypass]
Neurosurgery [intracranial or spinal]
Permanent pacemaker insertion or internal defibrillator placement
Selected invasive procedures [kidney biopsy, prostate biopsy, cervical cone biopsy, pericardiocentesis]
Spinal/epidural anesthesia

Intermediate

Other intraabdominal, intrathoracic, orthopedic or vascular Surgery

If on **warfarin**, go to **Step 2**, then **Step 3**
If on **NOACs**, go to **Step 3** (No bridging)

High (>10%/yr TE risk) → **Bridge with LMWH/UFH**

Mechanical Heart Valve (MHV)	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (< 6 mo) stroke/TIA
Atrial Fibrillation (AF)	• $CHADS_2$ of 5 or 6 • Recent (<3 mo) stroke/TIA • Rheumatic valvular heart disease
Venous Thrombo-embolism (VTE)	• Recent (<3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities

May also include those with a prior stroke/TIA occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery)

Moderate (5-10%/yr TE risk) → **Bridging is optional**

MHV	• Bileaflet aortic valve prosthesis + ≥ 1 RF: AF, prior stroke/TIA, HTN, DM, HF, age > 75 y
AF	• $CHADS_2$ of 3 or 4
VTE	• VTE within past 3-12 mo; Recurrent VTE • Nonsevere thrombophilia (eg heterozygous factor V Leiden or prothrombin gene mutation) • Active cancer (treated within 6 mo or palliative)

Low (<5%/yr TE risk) → **No bridging**

MHV	• Bileaflet aortic valve prosthesis without AF + no stroke RF
AF	• $CHADS_2$ < 3 (assuming no prior stroke/TIA)
VTE	• VTE > 12 mo previous + no other RF

For **High/Intermediate** procedure bleeding risk (Thrombosis Canada)

WARFARIN[1,2]	NOACs	
PRE-OP & POST-OP	PRE-OP	POST-OP
Day -5: stop warfarin **Day -3:** if bridging, start IV UFH/LMWH **Day -1:** INR testing (if INR >1.5, give vitamin K1 1-2 mg PO); if bridging, stop LMWH on the AM before Sx (omit PM dose if BID dosing; ↓ total daily dose by 50% with OD dosing) **Day 0:** if bridging, stop UFH 4-6 hrs before Sx; resume warfarin 12-24 hours after Sx if pt drinking fluids **Day +1 to +3:** if bridging, resume UFH/LMWH when hemostasis secured & not earlier than 12 hours after surgery; resume warfarin when patient drinking fluids **Day +5,+6:** if bridging, stop UFH/LMWH when INR therapeutic	**Apixaban** (BID) *(skip 4 doses)* Last dose: 3 days before Sx	**Apixaban** Resume 2 days after Sx
	Dabigatran (BID) CrCl > 50mL/min *(skip 4 doses)* Last dose: 3 days before Sx CrCl 30-50mL/min *(skip 6-8 doses)* Last dose: 4-5 days before Sx	**Dabigatran** Resume 2 days after Sx
	Rivaroxaban (OD) *(skip 2 doses)* Last dose: 3 days before Sx	**Rivaroxaban** Resume 2 days after Sx

Bridging Dose Regimens & Recommendations

Therapeutic Dose {most evidence}

1. **Enoxaparin**[Lovenox] 1 mg/kg SC BID or 1.5 mg/kg SC daily or
2. **Dalteparin**[Fragmin] 100 IU/kg SC BID or 200 IU/kg SC daily or
3. **Tinzaparin**[Innohep] 175 IU/kg SC daily; or
4. **Unfractionated Heparin (UFH)** IV to attain aPTT 1.5-2 X aPTT[control]

Enoxaparin, dalteparin, tinzaparin are covered under **Exceptional Access Program's (EAP) Telephone Request Service (TRS)** for **peri-operative bridging**, maximum of 10 days before date of surgery plus up to 7 days after surgery. Phone: 1-866-811-9893, Fax 1-866-811-9908