County of Los Angeles **Department of Health Services**

Los Angeles County Department of Health Services
PRACTICE GUIDELINE

SUBJECT/TITLE: Perioperative management of adult patients on oral anticoagulants

PURPOSE: To provide evidence-based guidelines for the perioperative management of oral anticoagulation therapy. These guidelines are intended to assist providers in managing anticoagulation in most clinical situations. They should not replace provider judgment or expert consultation.

ABBREVIATIONS:

VKA – vitamin K antagonist
IV – intravenous
APLS – antiphospholipid syndrome
AF – atrial fibrillation
VTE – venous thromboembolism
TIA – transient ischemic attack
CrCl – creatinine clearance
EF – ejection fraction
LMWH – low molecular weight heparin
UFH – unfractionated heparin
DOAC – direct oral anticoagulant

GUIDELINES:

Introduction:

Perioperative management of anticoagulation involves determining:

1. Whether anticoagulation needs to be interrupted in order to perform the procedure
2. When to discontinue the anticoagulant prior to the procedure
3. When to resume the anticoagulant after the procedure, and
4. Whether the use of bridging therapy is indicated

Bridging therapy refers to the use of a parenteral anticoagulant (low molecular weight heparin or IV unfractionated heparin) to maintain therapeutic anticoagulation during interruption of an oral anticoagulant.

This practice guideline was developed to assist the clinician in determining appropriate management of anticoagulation in the perioperative period. The perioperative plan should be developed with input from the provider performing the procedure as well as the provider managing anticoagulation.

Decision to interrupt oral anticoagulation

- Most procedures require temporary interruption of oral anticoagulant therapy, whether with warfarin or a DOAC
- Some procedures have a minimal risk of bleeding and may be performed safely without interrupting anticoagulation. The suggested management for these procedures is summarized in the following table:

Table: Management of Oral Anticoagulants in Minimal Bleeding Risk Procedures*

Minimal Bleeding Risk Procedures	DOAC management	Warfarin management
Dental procedures (such as single and multiple extractions, minor oral surgery, and placement of dental implants)[i],[ii],[iii],[iv]	Options: • Continue DOAC without interruption • Postpone the usual daily dose of DOAC until after the procedure • Omit DOAC on the day of the procedure	Continue warfarin without interruption (consider checking an INR prior to the procedure)
Cataract surgery[v]	Optimal management unknown	
Joint aspiration or injections[vi],[vii]	Continue DOAC without interruption	
Cardiac device implantation[viii],[ix]	• Last dose of DOAC in the morning of the day prior to the procedure • Resume DOAC the day after the procedure	Consult with cardiologist. Warfarin can usually be continued without interruption for pacemaker and defibrillator implantation.

* The decision to continue anticoagulation during a procedure should be made jointly with the provider managing anticoagulation and the provider performing the procedure.

Perioperative Interruption of DOACs[x],[xi]

- Due to the rapid onset and offset of action of DOACs, bridging therapy is not recommended during their interruption
- Stop DOAC medications according to the tables below.
- DOACs can be resumed at the patient's usual dose when hemostasis is achieved (usually 1 day after low bleeding risk procedures and 2-3 days after high bleeding risk procedures)
- These are general guidelines; the provider and surgeon should incorporate their clinical judgement to determine appropriate patient-specific care

Interruption of DOACs for Neuraxial procedures:

- Neuraxial interventions (e.g., epidural catheters, lumbar puncture) are associated with an increased risk of bleeding complications
- DOAC therapy should be avoided while an indwelling catheter is in place
- See the table on the following page

Table: When to stop and restart Direct Oral Anticoagulants

	Low Bleeding Risk Procedure			High Bleeding Risk Procedure			Neuraxial Procedure		
Factor Xa Inhibitors (Rivaroxaban, Apixaban, Edoxaban)		**Stop**	**Restart**		**Stop**	**Restart**		**Stop**	**Restart**
	CrCl < 15	No data	Resume 24 hrs after procedure (i.e. postop day 1)	**CrCl < 15**	No data	Resume 48-72 hrs after procedure (i.e. postop day 2-3)	**Any CrCl**	72 hrs prior to neuraxial intervention	Resume 6 hrs after neuraxial catheter is removed
	CrCl 15-29	Stop 36 hrs		**CrCl 15-29**	Stop 72 hrs (i.e. last dose evening of preop day 4)				
	CrCl ≥ 30	Stop 24 hrs (i.e. last dose evening of preop day 2)		**CrCl ≥ 30**	Stop 48 hrs (i.e. last dose evening of preop day 3)				
	Low Bleeding Risk Procedure			**High Bleeding Risk Procedure**			**Neuraxial Procedure**		
Direct Thrombin Inhibitors (Dabigatran)		**Stop**	**Restart**		**Stop**	**Restart**		**Stop**	**Restart**
	CrCl < 15	No data	Resume 24 hrs after procedure (i.e. postop day 1)	**CrCl < 15**	No data	Resume 48-72 hrs after procedure (i.e. postop day 2-3)	**CrCl < 30**	No data	Resume 6 hrs after neuraxial catheter is removed
	CrCl 15-29	Stop 72 hrs (i.e. last dose evening of preop day 4)		**CrCl 15-29**	Stop 120 hrs (i.e. last dose evening of preop day 6)				
	CrCl 30-49	Stop 48 hrs (i.e. last dose evening of preop day 3)		**CrCl 30-49**	Stop 96 hrs (i.e. last dose evening of preop day 5)		**CrCl 30-49**	Stop 120 hrs (i.e. last dose evening of preop day 6)	
	CrCl 50-79	Stop 36 hrs (i.e. last dose morning of preop day 2)		**CrCl 50-79**	Stop 72hrs (i.e. last dose evening of preop day 4)		**CrCl 50-79**	Stop 96 hrs (i.e. last dose morning of preop day 5)	
	CrCl ≥ 80	Stop 24 hrs (i.e. last dose evening of preop day 2)		**CrCl ≥ 80**	Stop 48 hrs (i.e. last dose evening of preop day 3)		**CrCl ≥ 80**	Stop 72 hrs (i.e. last dose evening of preop day 4)	

Perioperative Interruption of warfarin

- Given warfarin's long half-life, advanced planning for anticoagulation interruption is recommended for planned procedures.
- Stop and restart warfarin according to the table below
- The provider should consider the patient's thrombotic risk to determine if bridging therapy is indicated during warfarin interruption

When to stop and restart warfarin:		
	Usual timing:	Considerations:
STOP	5 days prior to the procedure	- Warfarin may be held for longer or shorter durations depending on the current INR, the time to the scheduled procedure, and the desired INR for the procedure - A provider can consider checking an INR 24 hours prior to the procedure to ensure INR is at or close to the desired level.
RESTART	Within 24 hours after procedure	- Due to its slow onset of action, warfarin can typically be resumed **within 24 hours** post-procedure at the patient's regular therapeutic dose. - In the setting of post-procedural bleeding complications or high post-procedural bleeding risk, provider may consider delaying warfarin resumption. This should be determined in consultation with the managing care team and the provider performing the procedure.

Thrombotic risk stratification for patients on warfarin[xii],[xiii],[xiv]

- Bridging therapy is **recommended** for patients with **high thrombotic risk conditions**, unless the risk of bleeding outweighs the benefit of bridging. High thrombotic risk conditions include:

High Thrombotic Risk Conditions:	
Mechanical Heart Valve	• Mechanical mitral valve • Caged-ball or tilting disc valve • Recent stroke/TIA (< 3 mos)
Atrial Fibrillation	• Recent stroke/TIA (< 3 mos) • Presence of cardiac thrombus • Rheumatic heart disease • CHA2DS2-VASc score ≥ 7
VTE	• Recent (< 3 mos) VTE • Presence of APLS • Strong genetic thrombophilia: - Protein C or S deficiency - Antithrombin deficiency - Homozygous factor V Leiden or PT gene mutations - Multiple abnormalities

- Bridging therapy is **not recommended** for patients with **low thrombotic risk conditions**, including:

Low Thrombotic Risk Conditions:	
Mechanical Heart Valve	• Bileaflet aortic valve with: - No atrial fibrillation, and - No history of stroke/emboli
Atrial Fibrillation	• Nonvalvular AF with: - CHA2DS2-VASc 1-4, and - No cardiac thrombus, and - No history of stroke/emboli
VTE	• VTE ≥ 12 months old, with: - No APLS, and - No genetic thrombophilia

- Patients with **moderate thrombotic risk** (i.e.: patients with conditions not specifically listed in the previous two sections) need **individualized consideration** to determine if bridging therapy is indicated.

Parenteral bridging

- Parenteral agents commonly used for perioperative bridging include low molecular weight heparin (LMWH) and IV unfractionated heparin (UFH)
- The decision to use UFH rather than LMWH as the bridging agent depends on renal function and the clinical setting (inpatient versus outpatient)

How to choose a parenteral bridging agent:	
LMWH	- Preferred agent for patients with CrCl > 30mL/min - Dose-adjusted LMWH can be considered for patients with CrCl between 15-30 mL/min
UFH	- Preferred agent for patients with CrCl < 30mL/min or when quick onset/offset of anticoagulation is desired - For UFH dose titration, please refer to the heparin policy and procedure
Other	For patients with an active or remote history of heparin allergy or heparin-induced thrombocytopenia, an alternative non-heparin anticoagulant should be selected with specialist consultation

Table: When to stop and restart parenteral bridging agents (LMWH and UFH)

Pre-procedure:	
START	- Inpatient: start parenteral agent once INR is below therapeutic range - Outpatient: start parenteral agent once INR is below therapeutic range **or** after omitting 2-3 doses of warfarin if the INR is not measured
STOP	- Discontinue LMWH at least 24 hours prior to the procedure - Discontinue UFH at least 6 hours prior to the procedure
Post-procedure:	
RESUME	Restart LMWH or UFH when adequate hemostasis is achieved
STOP	Discontinue LMWH or UFH when INR is therapeutic

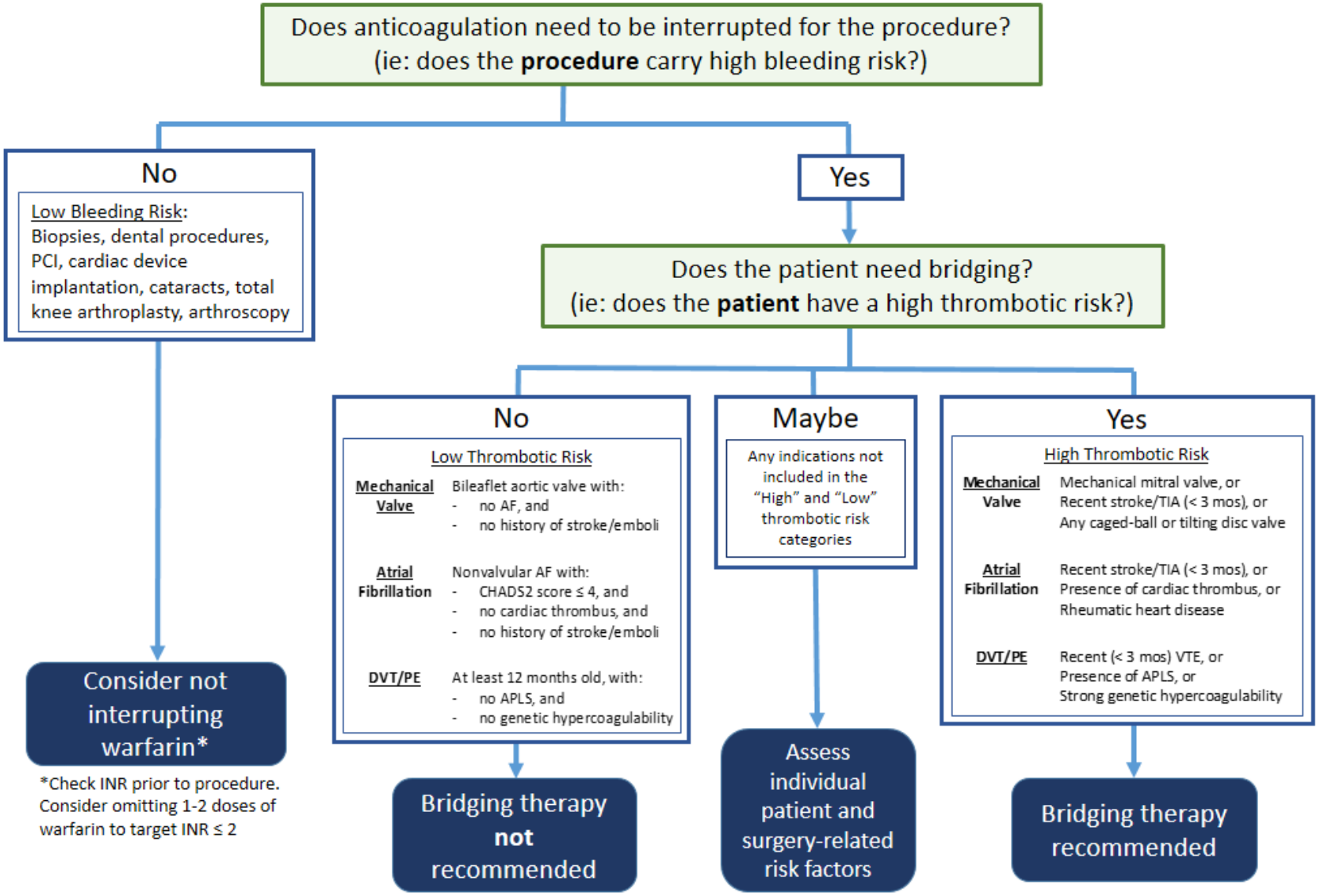
Appendix A: Thrombotic Risk Stratification for Patients on Warfarin

		Periprocedural Thrombotic Risk		
		High	**Moderate**	**Low**
Clinical Indication for warfarin therapy	**Mechanical heart valve**	• Mechanical mitral valve • Caged-ball or tilting disc valve • Recent stroke/TIA (within 3 mos)	• Bileaflet aortic valve with additional risk factors: - Atrial fibrillation - Prior stroke/emboli - Low EF (<30%)	• Bileaflet aortic valve with: - No atrial fibrillation, and - No history of stroke/emboli
	Atrial Fibrillation	• Recent stroke/TIA (within 3 mos) • Presence of cardiac thrombus • Rheumatic heart disease • CHA2DS2-VASc score ≥ 7	• Nonvalvular AF with: - CHA2DS2-VASc 5-6, or - History of stroke/emboli	• Nonvalvular AF with CHA2DS2-VASc 1-4, and - No cardiac thrombus, and - No history of stroke/emboli
	DVT/PE	• Recent (< 3 mos) VTE • Presence of APLS • Strong genetic thrombophilia, including: - Protein C or S deficiency - Antithrombin deficiency - Homozygous factor V Leiden or PT gene mutations - Multiple abnormalities	• VTE within 3-12 mos • Nonsevere thrombophilia • History of recurrent VTE • Active cancer	• VTE more than 12 months old, with: - No APLS, and - No genetic thrombophilia
Bridging Recommendation		Bridging therapy is **recommended** for patients with **high thrombotic risk conditions,** unless the risk of bleeding outweighs the benefit of bridging.	**Individualized consideration** is needed for patients with **moderate thrombotic risk**. May consult with anticoagulation management service or other subspecialty if desired.	Bridging therapy is **not recommended** for patients with **low thrombotic risk conditions**

Abbreviations: APLS – antiphospholipid syndrome AF – atrial fibrillation TIA – transient ischemic attack
VTE – venous thromboembolism EF – ejection fraction

References: Chest, ACC/AHA mechanical valves, ACC/AHA nonvalvular AFib, UW Medicine, Bridge AF

Appendix B: Decision Tree for Periprocedural Management of Warfarin



References:

[i] Jacobs Weltman N, Al-Attar Y, Cheung J, et al. Management of dental extractions in patients taking warfarin as anticoagulant treatment: A systematic review. J Can Dent Assoc 2015;81:f20.

[ii] Madrid C, Sanz M. What influence do anticoagulants have on oral implant therapy? A systematic review. Clin Oral Implants Res. 2009 Sep;20 Suppl 4:96-106.

[iii] Oral Health Topics: Anticoagulant and Antiplatelet Medications and Dental Procedures. https://www.ada.org/en/member-center/oral-health-topics/anticoagulant-antiplatelet-medications-and-dental- Accessed 1/24/2019

[iv] Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. European Heart Journal. 2018. Vol 39 (16): 1330–1393

[v] Jamula E , Anderson J , Douketis JD . Safety of continuing warfarin therapy during cataract surgery: a systematic review and meta-analysis. *Thromb Res*. 2009; 124 (3): 292 - 299.

[vi] Ahmed I, Gertner E. Safety of arthrocentesis and joint injection in patients receiving anticoagulation at therapeutic levels. Am J Med. 2012;125(3):265-269.

[vii] Yui JC, Preskill C, Greenlund LS. Arthrocentesis and joint injection in patients receiving direct oral anticoagulants. Mayo Clin Proc. 2017;92(8): 1223-1226

[viii] Birnie DH, Healey JS, Wells GA, et al. Pacemaker or defibrillator surgery without interruption of anticoagulation. N Engl J Med. 2013 May 30;368(22):2084-93.

[ix] Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. European Heart Journal. 2018. Vol 39 (16): 1330–1393.

[x] Doherty JU, Gluckman TJ, Hucker WJ, Januzzi Jr. JL, Ortel TL, Saxonhouse SJ, Spinler SA. 2017 ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation. J Am Coll Cardiol 2017;69:871–98

[xi] Douketis JD, Lip GY. Perioperative management of patients receiving anticoagulants. In J Tirnauer, L Leung (Eds.) *UpToDate*. Available from https://www.uptodate.com/contents/perioperative-management-of-patients-receiving-anticoagulants?search=perioperative%20anticoagulation&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed June 6, 2019.

[xii] Douketis JD, Spyropoulos AC, Spencer FA, et al; American College of Chest Physicians. Perioperative management of antithrombotic therapy: American College of Chest Physicians evidence-based clinical practice guidelines (9th edition). *Chest* 2012 ; 141(2)(suppl):e326S-e350S

[xiii] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2017;135:e1159–e1195.

[xiv] Doherty JU, Gluckman TJ, Hucker WJ, Januzzi Jr. JL, Ortel TL, Saxonhouse SJ, Spinler SA. 2017 ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation. J Am Coll Cardiol 2017;69:871–98