Kaiser Permanente NCAL
Perioperative Anticoagulation Management Guidelines

I. PURPOSE

To provide guidelines for the use of Anticoagulants including, but not limited to warfarin and low molecular weight heparin (LMWH, or Enoxaparin) as part of an outpatient management program for patients who require a surgical or other invasive procedures. Outpatient Anticoagulation Service (OACS) currently only manages patients on warfarin therapy. Peri-op management of other anticoagulants and anti-platelets is the responsibility of patient's treating physician.

II. GOALS/OBJECTIVES

To provide safe and effective medication therapy management for patients before and after surgery or other invasive procedures

NOTE: Due to lack of prospective data and individual variability in risk for thrombosis and bleeds, perioperative anticoagulation management remains controversial. Individual provider-patient decisions may differ from the guideline below. Clinical judgment must be exercised.

III. PROCESS

Physicians and Surgeons Responsibilities:

1. Inform Outpatient Anticoagulation Service (OACS) of the planned procedure including type of procedure, date of procedure, and any specific instructions outside of this guideline using CC Chart in HealthConnect to OACS pool address "p *** coag pha" (refer to SECTION VI for complete address). Elective procedures may need to be postponed if OACS are not notified at least 1 week in advance to coordinate bridging plan.
2. Notify OACS via CC Chart if a physician desires to modify the patient's perioperative anticoagulation plan, generated by the Anticoagulation Service Pharmacist. Consider sending E-Consult to Anticoagulation Service for problem/reason of "Perioperative Bridging".
3. Instruct patient on resumption of warfarin/LMWH therapy after procedure when adequate hemostasis is obtained and inform Anticoagulation Service via CC chart.
4. Notify OACS via CC Chart when discontinuing patient's perioperative anticoagulation therapy post procedure.
5. Instruct patient on holding parameters for non-warfarin oral anticoagulation such as Dabigatran and antiplatelet therapy such as aspirin, clopidogrel (Plavix), dipyridamole/asa (Aggrenox).
6. For patients on warfarin, recommend pre-op INR check one day prior to procedure and treat with vitamin K tablet 2.5 mg orally if INR $\geq$ 1.5 when deemed appropriate.
7. POM will make sure that patients on chronic warfarin has a perioperative bridge plan documented in KPHC under "**Peri-op Anticoagulation Management Plan** " and will notify OACS via CC Chart if it is not present..

Outpatient Anticoagulation Service (OACS) Pharmacist Responsibilities:

1. Once OACS is notified, pharmacist will clinically assess the patient's thromboembolic risk and the bleeding risk associated with the procedure, and then draws out a plan for the patient's perioperative anticoagulation therapy based on the clinical guidelines for perioperative bridging.
2. Pharmacist will inform the surgeon, primary care physician, and POM of the perioperative bridging plan via CC Chart. Pharmacist will document procedure plan in an encounter using chief complaint of **"Peri-op Anticoagulation Management Plan" ID 3259**. If a physician desires to modify the plan based on their knowledge of the patient's clinical status, he or she will notify OACS via CC Chart.
3. Pharmacist will monitor PT/INR, provide patient with appropriate daily warfarin and low molecular weight heparin (LMWH) dosage, and discontinue LMWH when therapeutic INR is reached and/or no longer indicated.
4. Pharmacist will order subcutaneous LMWH. Pharmacist will coordinate teaching of LMWH for patient or their caregiver of LMWH administration. In the event that patient is not able to self inject LMWH, pharmacist will coordinate for patient to receive the injections.
5. Patients requiring bridge therapy with LMWH will receive an outpatient perioperative anticoagulation bridge therapy letter generated using HealthConnect.
6. Pharmacist may instruct patient on resumption of warfarin/LMWH therapy <u>after</u> procedure based on the clinical guidelines for perioperative bridging in the event that patient is unclear of post-procedure instructions. Pharmacist will inform the surgeon, referring physician, and/or POM of the plan using HealthConnect.

Inclusion Criteria:

- Patients who require interruption in warfarin therapy for invasive procedures or diagnostic tests and are currently enrolled in the Outpatient Anticoagulation Services.

Exclusion Criteria:

Patients with any of the following conditions should be excluded from these guidelines and managed on a case-by-case basis:

- Age < 18 years
- Active major bleeding
- Physician desires to modify the protocol for their individual patient
- Patients with conditions or undergoing procedures <u>not</u> found in the clinical guidelines and recommendations for perioperative bridging

Caution: Consult Responsible Provider

1. Creatinine clearance / GFR less than 15 ml/minute
2. Obese patients with weight > 150 kg, consider Anti- Xa monitoring
3. Hypersensitivity to LMWH, consider other parenteral anticoagulant (i.e. Fondaparinux)
4. History of documented heparin-induced thrombocytopenia (HIT)

IV. CLINICAL GUIDELINES AND RECOMMENDATIONS

1. Enoxaparin (Lovenox) dosing for Perioperative Bridge Therapy

After carefully assessing the thromboembolic risk and the bleeding risk, Pharmacist will use the Bridge Therapy Algorithm to determine the dose of enoxaparin to use for perioperative bridging therapy:

a. Therapeutic dose of enoxaparin for perioperative bridging therapy. Dose should be calculated using actual body weight (ABW):

i. Once Daily Dose = 1.5 mg/kg, round to the nearest syringe size
ii. Twice Daily Dose = 1 mg/kg, round to the nearest syringe size
iii. CrCl/GFR < 30 ml/min: 1 mg/kg once daily, round to the nearest syringe size but not more/less than 5%

b. Prophylactic dose of enoxaparin for perioperative bridging therapy:

i. Once daily dose = 40 mg
ii. Twice daily dose = 30 mg
iii. CrCl/GFR less than 30 ml/min: 30 mg once daily

Enoxaparin is available in 30, 40, 60, 80, 100, 120, 150 mg/ml syringe sizes. Please refer to detailed dosing instructions on twice daily and once daily dosing of enoxaparin in timeline attached as Appendix A & B.

NOTE: Consideration for once daily vs. twice daily dosing is based on many patient specific factors. Once daily dosing may improve compliance and it is more practical for patients who need to come into the medical center for their injections. Twice daily regimen may be considered for patients who are at higher risk for thromboembolic events and are able to self inject reliably twice daily. For example, patients with mechanical mitral valves or patients with Atrial Fibrillation with recent stroke/TIA within 3 months may be considered for twice daily dosing regimen.

Patients with a history of HIT need to be evaluated regarding risk vs. benefit of a simple warfarin hold with no bridging for necessary procedures. If bridging is needed, consider the use of non-heparin agents like lepirudin (Refludan), argatroban (Novastan), and fondaparinux (Arixtra). There is no data available to date regarding the safety for non-heparin agents in perioperative management. Consult the responsible provider.

2. Perioperative recommendations for Dabigatran (Pradaxa) (managed by treating physicians)

Dabigatran (Pradaxa)

a. LMWH bridging is currently not recommended for patients on dabigatran
b. There is currently no clinical evidence for the use of dabigatran in patients with CrCl < 30 ml/min. Therefore, the use of dabigatran in this patient population is currently not recommended. If dabigatran is being used in patients with CrCl 15 -30 ml/min, the FDA recommends dose reduction to 75mg orally BID based on pharmacokinetics.

c. Dabigatran is contraindicated in patients with CrCl < 15 ml/min

d. Recommend measuring activated partial thromboplastin time (aPTT) pre-op. Dabigatran has been shown to prolong aPTT by increasing peak level by 2x control and median trough level by 1.5x control approximately.

e. Restart dabigatran once hemostasis has occurred post procedure

Pre-op Recommendations for dabigatran (Pradaxa) hold		
Renal Clearance (CrCl in ml/min)	**High Bleeding Risk***	**Standard Bleeding Risk**
50	Hold 3 days prior	Hold 1 day prior
> 30 to < 50	Hold 4 days prior	Hold 2 days prior
≤ 30	Hold 5 days prior	Hold 2 to 5 days prior
• * High bleeding risk includes major surgery, spinal puncture / epidural catheter, or in whom complete hemostasis may be required. • If Dabigatran is held for more than 2 days in patients with normal renal functions and more than 4 days in patients with reduced renal functions, please consult the treating physician or the cardiologist to decide on the need for Bridge therapy. NOTE: Check aPTT prior to procedure to ensure dabigatran has been cleared from the system.		
References: 31, 32		

3. Perioperative recommendations for Antiplatelet drugs (managed by physicians)

CAUTION: Patients with Coronary Stents

In patients with coronary stents, please do not stop antiplatelet medications (e.g. **aspirin, thienopyridine, clopidogrel, prasugrel, ticagrelor) without consulting patient's cardiologist.**

- Defer all elective surgeries for at least 4 weeks after placement of bare metal stent and 12 months for drug eluting stent.
- Elective surgery may be considered earlier if 1) the surgery can be performed on aspirin and thienopyridine, and 2) the cardiac risk has been discussed with cardiology

For further information, refer to Perioperative Medicine Guidelines 2012 Antiplatelet Management in Coronary Stents".

Recommendations for Perioperative Management of Aspirin		
Type of Procedures	**Cardiovascular (CV) Risks**	**Recommendation (grade 2C)**
Low bleeding risk procedures Dental, Dermatologic, Cataract, etc.	ASA for secondary prevention of CV disease	Continue ASA during procedure
Surgery associated with increased risk for cardiovascular events: Carotid endarterectomy Peripheral Artery Bypass Surgery CABG*	N/A	Continue ASA during procedure *For CABG: For patients on dual antiplatelet, continue ASA, and stop clopidogrel 5 days and prasugrel 7 days before surgery
Noncardiac surgery**	**Moderate to high risk for CV events such as patients with:** Coronary Artery Disease Ischemic Heart Disease Cerebrovascular Disease	Continue ASA during procedure **Intracranial / Prostate surgery and extremely high bleeding risk procedure, may consider stopping ASA with caution depending on CV risk
	Low Risk for CV events	Consider interruption of ASA 7 -10 days before surgery

*****Recommended pre-procedure washout period for antiplatelets***

Antiplatelets	**Pre-procedure washout**
Aspirin	7-10 days
Cilostazol (Pletal®) *NF*	2-3 days
Clopidogrel (Plavix®)	5-7 days
Dipyridamole (Persantine®)	2-3 days
Dipyridamole/aspirin (Aggrenox®)	7-10 days
Prasugrel (Effient®)	7 days
Ticagrelor (Brilinta®) *NF*	5 days
Ticlopidine *NF*	10-14 days

Table 1: Risk stratification for thromboembolism to decide on LMWH Bridge

a. Patients with low thromboembolic risk do not require any LMWH Bridge
b. Patients with high thromboembolic risk will require LMWH Bridge

Table 1: Risk Stratification for Perioperative Thromboembolism		
	HIGH	**LOW**
Valvular Heart Disease	• All **mitral** valve prosthesis • Older generation (caged-ball or tilting disc) **aortic** valve prosthesis • Bileaflet **aortic** valve prosthesis with risk factors for stroke/TIA* • Bileaflet **aortic** valve prosthesis with AF	• Bileaflet **aortic** valve prosthesis without risk factors for stroke*
Atrial Fibrillation	• Chronic AF with prior stroke or TIA • History of LV thrombus • Rheumatic Valve Disease • EF < 30%	• Chronic AF with no prior stroke or TIA
Venous Thromboembolism	• Recent VTE within the past 12 months • History of VTE AND other risk factor(s)** **MODERATE TO LOW RISK** • Recurrent VTE > 12 months without any other risk factors, consider using LMWH Prophylactic Dose	• Single unprovoked VTE > 12 months ago and no risk factors**

*__Risk factors for Stroke/TIA:__ acute congestive heart failure within 100 days, hypertension, age ≥ 75 years, diabetes, and history of stroke or TIA

**__Risk factors for VTE__: Deficiency of protein C, protein S, or antithrombin, antiphospholipid antibody syndrome, homozygous factor V leiden mutation, IVC filter, and active cancer

AF= Atrial Fibrillation, LV=Left Ventricular, TIA = Transient Ischemic Attack, VTE= Venous Thromboembolism.
NOTES:

- Please consult the cardiologist for patients with double mechanical valves or combined AF, mitral valve prosthesis and severe LV dysfunction with EF < 30% to consider the use of IV unfractionated heparin (UFH) as inpatient and stop Heparin 4 -6 hours before surgery.
- Elective procedures should be postponed in patients with acute VTE (within 3 months) and patients with coronary bare metal stent placed in past month or drug eluting stent in past 12 months.
- Single provoked VTE > 12 months ago should not be on warfarin

References: 1, 4, 6, 7, 16, 17, 19 and 20

Version 2 approved by KP NCAL Regional P&T on August 24th 2012

Table 2: Bleeding risk associated with surgeries or invasive procedures

a. High bleeding risk procedures will require warfarin hold for five days prior to the procedure. Low bleeding risk procedures do not require warfarin hold prior to the procedure
b. Providers will notify OACS when a patient is scheduled for procedure and when to restart anticoagulation therapy after the procedure via CC Chart to OACS pool address
c. OACS pool addresses (p *** coag pha) are located in section VI of this document. For example, San Francisco OACS pool address is "p sfo coag pha"

Table 2: Bleeding Risk Associated with Different Types of Procedures * *For major procedures when risk of bleeding is high, may hold resumption of anticoagulation therapy for 48 to 72 hours post-op until the high risk of bleeding abates. For all other procedures, may resume 24 hours once hemostasis has occurred.	
HIGH	**LOW**
Cardiology/vascular procedures: All cardiac procedures are considered high risk	
All cardiac procedures (including pacemaker implantation, adjustment or battery replacement, Implantable cardioverter-defibrillator implantation, cardiac catheterizations, angiograms, valve replacements)	
Gastroenterological procedures	
Gastroenterologists will assess bleeding risk post procedure and inform OACS via "CC Chart" to pool address when to resume anticoagulation therapy post procedure. GI schedulers will also send an e-consult when a procedure is scheduled on a warfarin patient for OACS to develop Periop plan.	
• Upper gastroesophageal endoscopy • Colonoscopy • ERCP • Laser ablation • Endoscopic sphincterotomy • Pneumatic or bougie dilation • Percutaneous endoscopic gastrostomy	• Flex sigmoidoscopy screening
Pain procedures	
• Epidural steroid injection • Sacroiliac joint injection • Facet medial branch blocks • Selective nerve root block	• Trigger Point Injection • Occipital Nerve blocks • Peripheral injections • Pump refills

• Stellate ganglion block • Disc procedures	
Urologic procedures: All urologic procedures are considered high risk	
In Urology, it is difficult to assess the bleeding risk till after the procedure. Hence the urologists have agreed to assess patient's individual bleeding risk post procedure and notify OACS via CC Chart to pool address when it is safe to resume anticoagulation therapy.	
• Transurethral resection of the prostate • Transurethral resection of the bladder tumor (TURBT) • Kidney, prostate or bladder biopsy • Partial nephrectomy • Ureteroscopy	
General, Thoracic and Plastic Surgery	
• All major thoracic, abdominal and pelvic Surgeries • Surgeries and procedures in kidney, liver, spleen • Bowel resection • Cancer surgeries • Reconstructive plastic surgeries	• Excision of subcutaneous nodules less than 3 CM
Gynecological procedures: Hold warfarin for all procedures except low risk procedure listed	
	• Vulvar biopsy. • Laser of vulva, vagina. • Leep of cervix • D and C • Hysteroscopy, diagnostic • Ablation- HTA or thermachoice only (not resectoscopic)
Orthopedics, Neurologic, and Spinal Procedures	
• Total joint replacement surgeries – mainly in hip, knee, or shoulder • Fracture repair in femur, humerus or pelvis • Intracranial and Spine surgeries	• Joint, bursa, and tendon sheath aspirations and injections
Podiatry Procedures	
• Surgical osteotomies • Open reduction/internal fixation foot and ankle fractures/dislocations	• OFFICE PROCEDURES-including: nail procedures, wart removal, foreign body (superficial), skin biopsy (superficial)

• Soft tissue/mass excision • Arthrodesis of the toes/foot/ankle • Arthroscopy-foot/ankle • Removal foreign body (deep) • Tendon repair • Neuroma/neurectomy • Close reduction (DISCLAIMER: may times we will need to convert to an open reduction and hence they will need to be off of warfarin) • Biopsies-skin (deep), fascia, muscle bone	• Removal external fixation

Dermatology procedures: All dermatologic procedures are considered low risk including Mohs surgery and simple excisions

Ophthalmology procedures

It is difficult to predict the bleeding risk in ophthalmic procedures. Ophthalmologists agreed to assess patient's individual bleeding risk post procedure and notify OACS via "CC Chart" of when it is safe to resume anticoagulation therapy.

• Trabeculectomy with/without cataract extraction • Trabectome Surgery • Bleb revision • Glaucoma Tube Shunt Implants • Ahmed Implant • Baerveldt Implant • All Oculoplastic/Reconstructive • Blepharoplasty • Entropion/Ectropion Repair • All Orbital Surgery • Dacryocystorhinostomy (DCR)	• Cataract extraction with IOL implantation • Endocyclophotocoagulation • Glaucoma laser / other lasers • Refractive Laser Surgeries • LASIK, PRK • Corneal Surgeries • Cornea Transplant • DSEK, DLEK • Retrobulbar Anesthesia**

**While Retrobulbar anesthesia carries a risk of retro-orbital hemorrhage, the consensus of opinion from the Regional Chiefs of Ophthalmology is that it poses a low risk for bleeding and does not require holding anticoagulation. In addition, the Chiefs of Ophthalmology strongly recommend topical anesthesia for cataract extraction which poses no risk of bleeding.

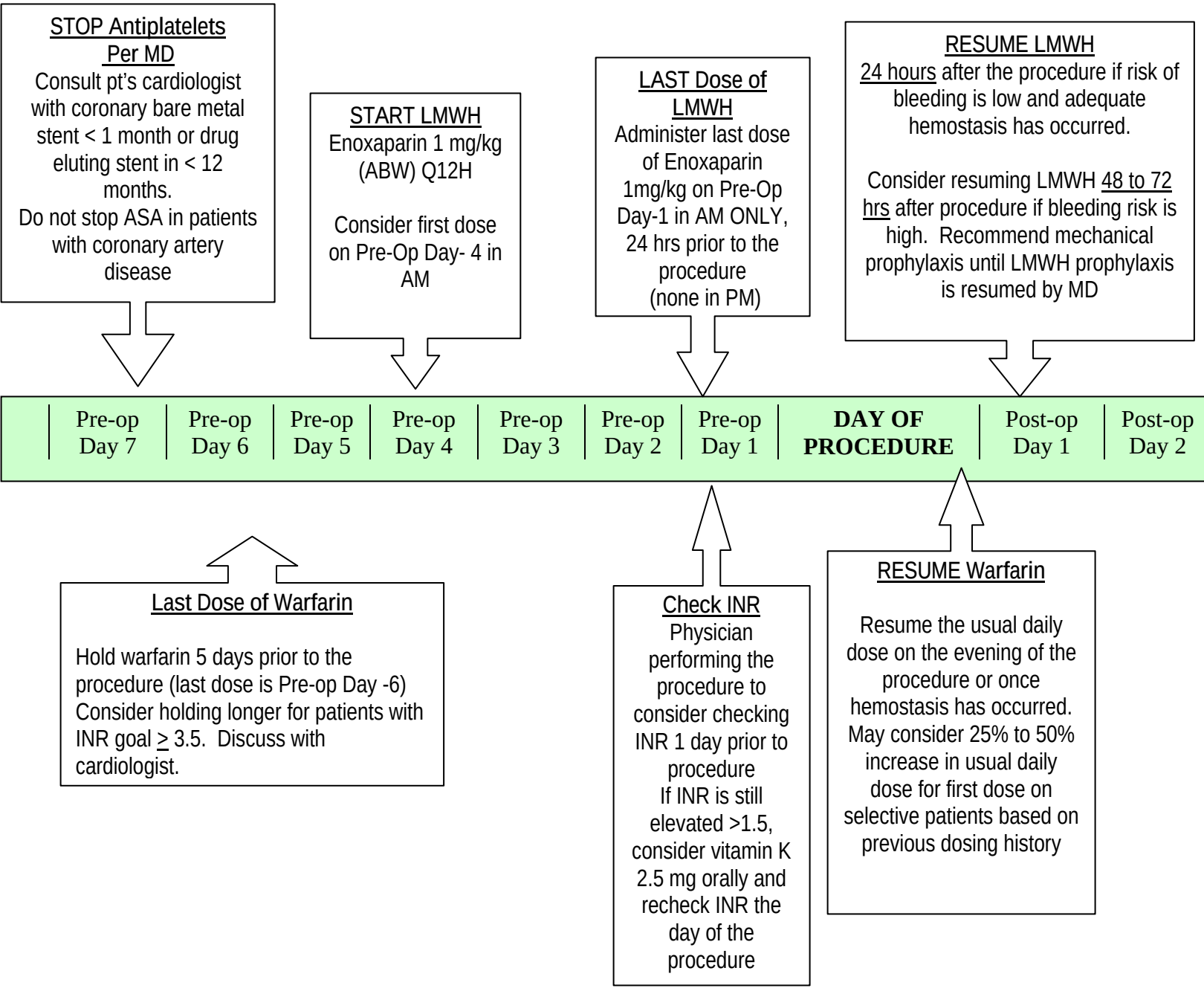
References: 1,2

Consensus agreements from various Chiefs groups including Cardiology, Gastroenterology, Interventional Pain management, Opthalmology, Urology, Orthopedics, Podiatry, General Surgery, Perioperative Medicine, Gynecology and Dermatology, 2010-2012.

Table 3: Perioperative anticoagulation plan Algorithm

Table 3: Bridge Therapy Algorithm		
	ACTION: PRE-OP	**ACTION: POST- OP**
Low Thromboembolic Risk	Hold warfarin 5 days prior to procedure. Last dose of warfarin on Pre-Op Day 6. No LMWH bridging	Resume warfarin once hemostasis has occurred • Resume at usual daily dose, the evening of surgery, or the next day once hemostasis has occurred. • May consider 25% to 50% increase in the first dose in selective patients based on previous dosing history
High Thromboembolic Risk	Hold warfarin 5 days prior to procedure. Last dose of warfarin on Pre-Op Day 6. If INR goal is > 3.0, consider holding warfarin 6 days prior to procedure. **Bridging Options** LMWH Therapeutic Dose: • Once Daily Regimen: Enoxaparin 1.5 mg/kg Q24h • Twice Daily Regimen: Enoxaparin 1 mg/kg Q12h **Start enoxaparin** First dose on the evening of Pre-Op Day 4 **Last dose of enoxaparin** • **Twice Daily Dosing Regimen** (Appendix A): Last dose on Pre-Op Day 1 with enoxaparin 1mg/kg in AM ONLY 24 hours prior to the procedure; none in PM • **Once Daily Dosing Regimen** (Appendix B): Last dose on Pre-Op Day 2 with enoxaparin 1.5mg/kg in evening (approximately 36 hours prior to procedure)	Resume warfarin once hemostasis has occurred • Resume at usual daily dose, the evening of surgery, or the next day once hemostasis has occurred. • May consider 25% to 50% increase in the first dose in selective patients based on previous dosing history Resume enoxaparin once hemostasis has occurred • **Low bleed risk**: 24 hrs after procedure • **High bleed risk**: 48-72 hrs after procedure OR longer as directed by surgeon or physician
NOTE: Patients with a history of recurrent VTE more than 12 months carry moderate to low risk and hence recommend prophylactic dose of LMWH for Bridging (Enoxaparin 30 mg Q12h or Enoxaparin 40 mg Q24h)		
References: 1, 2, 3, 4, 7, 8		

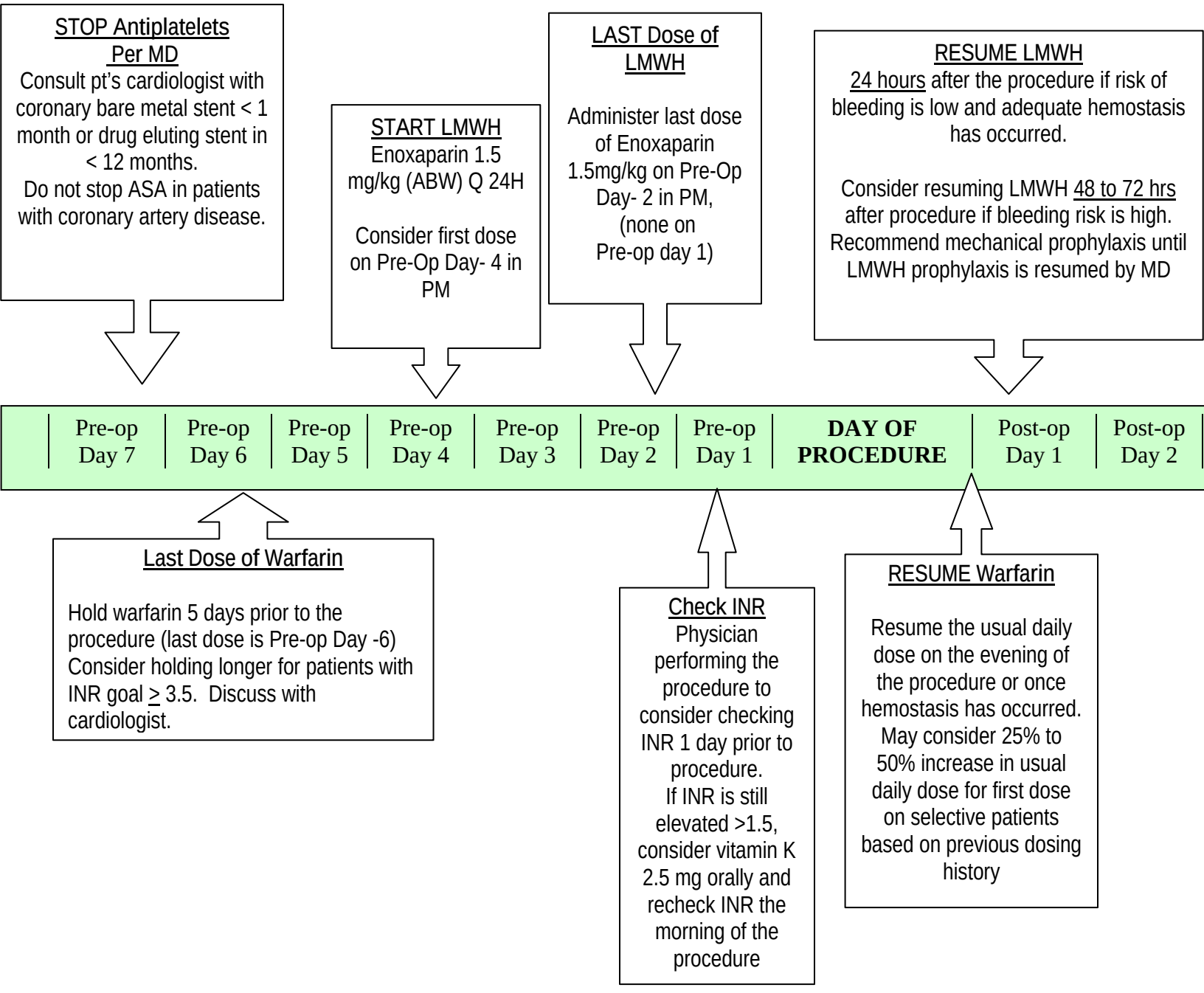
Appendix A: Guidelines for Perioperative Bridge Therapy Timeline with LMWH Twice Daily Dose



NF – non-formulary

Version 2 approved by KP NCAL Regional P&T on August 24th 2012

Appendix B: Guidelines for Perioperative Bridge Therapy Timeline with LMWH Once Daily Dose



Version 2 approved by KP NCAL Regional P&T on August 24th 2012

V. DENTAL PROCEDURES AND ANTICOAGULATION MANAGEMENT

a. Clinically significant bleeding is defined as bleeding that is unplanned and may be controlled using local measures. This is different from life threatening bleeding. Therefore, warfarin may still be continued for procedures that are considered high bleeding risk depending on patient's thromboembolic risks.

b. Stopping warfarin for dentoalveolar surgery is not supported by clinical evidence

c. Consider pre-procedural INR to ensure INR < 4.0

Table 4: Recommendations on Anticoagulation management for Dental Procedures

Bleeding Risk	Types of Procedure	Recommendations
LOW RISK	• Crown and bridge procedures • Multiple simple extractions • Periodontal exams, x-rays • Regional and local injections anesthetics • Restorations • Standard root canal • Sub-gingival scaling with inflamed gums • Supra-gingival scaling, root planning, endodontics • Surgical removal of teeth	• Do not interrupt warfarin therapy • Use local measures to prevent or control bleeding • Consider other dental options if concerned: o Limit 2-3 teeth (non-impacted, bony or soft tissue) extractions per dental appointment • Restrict scaling to one quadrant per visit and re-assess
MODERATE RISK	• Alveoloplasties • Apicoectomy (root removal) • Alveolar surgery (bone removal) • Dental implants • Full mouth extractions	• Same as above • Use extra caution
HIGH RISK	• Extensive surgery • Tori removal • Vestibuloplasty • Free gingival graft • Block bone graft	• Consider patient's risk for thromboembolic event. If low, then may consider adjusting warfarin dose • If risk of thromboembolism is high, then discuss with dentist and PCP. May consider adjusting warfarin dose
References:1, 22, 23, 24, 25, 26, 27, 28		

Suggested Clinical Interventions to Prevent and Control Bleeding after Dental Surgeries

- Site packing with an absorbable haemostatic dressing such as oxycellulose (Surgicel), collagen sponge (Haemocollagen), or resorbable gelatin sponge (Spongostan). Surgicel is preferred followed by direct pressure (i.e. instruct patient to bite on three or four gauze).
- Additional suturing using resorbable or non-resorbable sutures followed by pressure using a gauze pad for 20 minutes
- Electrocautery
- Topical thrombin powder
- Tranexamic acid mouth rinse 5% (provides little benefit when used in addition to other hemostatic dressing)

Suggested Patient Instructions to Prevent and Control Bleeding at home

- Cold ice pack applied extraorally (avoid water rinse as it may dissolve or loosen blood clot)
- Local pressure (biting on gauze or tea bags)
- Avoid the following for 24 hours after procedure: hot liquids, mouth washes, hard foods, and use of straws/sucking hard or disturb the socket with tongue or any foreign object

VI. Pool Address for Outpatient Anticoagulation Clinical Services

KP NCAL	Facility	Pool Name
CAM	Sacramento	P SAC COAG PHA
	South Sacramento	P SSC COAG PHA
CCM	Fresno	P FRS COAG PHA
	Central Valley	P STK COAG PHA
EBM	Oakland	P OAK COAG PHA
	Richmond	P OAK COAG PHA
	Greater Southern Alameda Area	P HAY COAG PHA
GGM	Marin-Sonoma	P SRF COAG PHA
	Redwood City	P RWC COAG PHA
	San Francisco	P SFO COAG PHA
	Santa Rosa	P SRO COAG PHA
	South San Francisco	P SSF COAG PHA
NBM	Diablo	P DSA COAG PHA
	Napa-Solano	P VAL COAG PHA
SBM	Santa Clara	P SCH COAG PHA
	San Jose	P STR COAG PHA

VII. REFERENCES:

1. Douketis JD, Spyropoulos, AC, Spencer, FA, et al. The Perioperative Management of Antithrombotic Therapy. *CHEST*. 2012; 141: S326-350S
2. Douketis JD, Berger PB, Dunn AS, et al. The Perioperative Management of Antithrombotic Therapy. *CHEST*. 2008; 133: 299S-339S
3. Clinical Pharmacology Web site. Available at: http://www.clinicalpharmacology-ip.com/. Accessed on November 8, 2009.
4. Grant PJ, Brotman DJ, Jaffer AK. Perioperative Anticoagulant Management. *Med Clin N Am.* 2009; 93: 1105-21.
5. Cannegieter SC *et al*. (1994) Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. *Circulation* 89: 635-641
6. Jaffer AK, Brotman DJ, Chukwumerije N. When patients on warfarin need surgery. *Cleveland Clinic Journal of Medicine.* 2003; 70(11): 973-84.
7. Kyrle PA, Eichinger S. Deep Vein Thrombosis. *Lancet*. 2005; 365: 1163-74
8. Dunn AS, Turpie AGG. Perioperative management of patients receiving oral anticoagulants. *Arch Intern Med*. 2003; 63: 901-8.
9. Heuts LM, McLendon BM, Cender DE. LMWH for perioperative anticoagulation in patients on chronic warfarin therapy. *Ann Pharmacotherapy*. 2004; 38: 1065-9.
10. Herman WW, Konzelman JL, Sutley SH. *J Am Dent Assoc.* Vol. 128, March 1997:327-335
11. Zinkovsky DA, Antonopoulos MS. Heparin-induced thrombocytopenia. *P&T*. 2008; 33(11):642-51
12. Herman WW, Konzelman JL, Sutley SH. *J Am Dent Assoc.* Vol. 128, March 1997:327-335 Am Heart J. 2004 Jan;147(1):3-15
13. J Am Dent Assoc. 2000 Jan;131(1):77-81
14. Oral Surg Oral Med Oral Pathol. 1993 Jan;75(1):29-31
15. Arch Intern Med. 1998 Aug 10-24;158(15):1610-6
16. Head Face Med. 2005 Nov 29;1:12
17. Jain A, Mazanek GJ, Armitage JM. Unstable Angina Secondary to Left Main Coronary Thrombus Extending from Prosthetic Aortic Valve. *Cathet Cardiovasc Diagn* 1988;15(4).271-272
18. Torella M, Torella D, Chiodini P, et al. Lowering the Intensity of Oral Anticoagulant Therapy in Patients with Bileaflet Mechanical Aortic Valve Replacement: Results from the "LOWERING-IT" Trial. *Am Heart J*, 2010 Jul; 160(1): 171-178
19. Ferreira I, Dos L, Tornos P, et al. Experience with Enoxaparin in Patients with mechanical heart Valves Who Must Withhold Acenocumarol. Heart 2003 May; 89:527-530
20. Spyropoulos AC, Turpie AGG, Dunn AS, et al. Perioperative Bridging Therapy with Unfractionated Heparin or Low-Molecular-Weight Heparin in Patients with Mechanical Prosthetic Heart Valves on Long-Term Oral Anticoagulants (from the REGIMEN Registry). *Am J Cardiol* 2008;102:883-889

21. Bui HT, Krisnaswami A, Le CU, et al. Comparison of the Safety of Subcutaneous Enoxaparin as Outpatient Anticoagulation Bridging Therapy in Patients with a Mechanical Heart Valve versus Patients with Nonvalvular Atrial Fibrillation. *Am J Cardiol* 2009;104:1429-1433
22. Shlebak A, Malik I. Managing Heparin Anticoagulation in Patients with Prosthetic Cardiac Valves: Balancing the Risk. *Heart* 2009;95:1643-1645
23. Herman WW, Konzelman JL, Sutley SH. *J Am Dent Assoc.* Vol. 128, March 1997:327-335, Am Heart J. 2004 Jan;147(1):3-15J Am Dent Assoc. 2000 Jan;131(1):77-81 Oral Surg Oral Med Oral Pathol. 1993 Jan;75(1):29-31
24. Nematullah, et al, Dental Surgery for Patients on Anticoagulant Therapy with Warfarin: A Systemic Review and Meta-analysis. JCDA February 2009, Vol. 75, No. 1
25. Christine Randall, Surgical Management of the Primary Care Dental Patient on Warfarin. North West Medicines Information Center: Pharmacy Practice Unit: Liverpool England. Revised 3/09.
26. University of Washington Medical Center Anticoagulation Service Guidelines
27. Andrew S. Dunn, MD; Alexander G. G. Turpie, MD, FRCP, Perioperative Management of Patients Receiving Oral Anticoagulants *Arch Intern Med.* 2003; 163:901-908.
28. O. Ross Beirne, DMD, PhD, Evidence to Continue Oral Anticoagulation Therapy for Ambulatory Oral Surgery. J. Oral Maxillofac Surg: 63: 540-545, 2005
29. Todd DW, Evidence to support an individualized approach to modification of oral anticoagulant therapy for ambulatory oral surgery. J Oral Maxillofac Surg. 2005 Apr;63(4):536-9.
30. Nutescu EA, et.al. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. Ann Pharmacother. 2009 Jun; 43(6):1064-83. Epub 2009 May 19.
31. Pradaxa (Package Insert). Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. October 2010
32. Connolly, Stuart, Ezekowitz, Michael, Yusuf, Salim et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. NEJM 2009: 361:1139-1151
33. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines. J. AM . Coll. Cardiol. 2006; 48; e149-e246. Available at http://content.onlinejacc.org/cgi/reprint/48/4/e149.pdf
34. Horlocker T, Wedel DJ, Rowlingson J, et al. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Regional Anesthesia and Pain Medicine. 2010. 35; p64-101. Available at http://www.asra.com/publications-anticoagulation-3rd-edition-2010.php
35. Horlocker, TT. "Regional anesthesia in the patient receiving antithrombotic and antiplatelet therapy." *British Journal of Anesthesia* 2011; 107(S1): i96-i106.