Table 3: WARFARIN INTERRUPTION AND BRIDGING SUGGESTIONS[1,2]

Day	Warfarin Dose	Bridging with Low Molecular Weight Heparin (LMWH)	International Normalized Ratio (INR) Monitoring
-7 to -10	Maintenance dose	Assess for perioperative bridging anticoagulation; classify patients as undergoing high or low bleeding risk procedures	Check baseline labs (hemoglobin, platelet count, serum creatinine, INR)
-6- or -5	Begin to hold warfarin day -5 or day -6	No LMWH	None
-4	No Warfarin	No LMWH	None
-3	No Warfarin	Start LMWH at therapeutic or intermediate dose†	None
-2	No Warfarin	LMWH at therapeutic or intermediate dose†	None
-1	No Warfarin	Last preprocedural dose of LMWH administered no less than 24 h before start of surgery at half the total daily dose	Assess INR before the procedure; proceed with surgery if INR <1.5; If INR > 1.5 and <1.8, consider low-dose oral vitamin K reversal (1-2.5 mg)
0 or +1	Resume maintenance dose of warfarin on evening of or morning after procedure	None	None
+ 1	Maintenance dose	Low-bleeding risk: restart LMWH at previous dose; High-bleeding risk: no LMWH administration;	Per clinician judgment
+2 or +3	Maintenance dose	Low-bleeding risk: LMWH administration continued High-bleeding risk: restart LMWH at previous dose	Per clinician judgment
+4	Maintenance dose	Low-bleeding risk: INR testing (discontinue LMWH if INR > 1.9) High-bleeding risk: INR testing (discontinue LMWH if INR > 1.9)	INR
+7 to +10	Maintenance dose		INR

Decisions to interrupt, bridge, and resume anticoagulants MUST be clearly communicated among providers and to patient.

Table 4: PERI-PROCEDURAL USE OF ANTIPLATELETS[3]

Patient Population on Antiplatelet	Action
On aspirin for secondary prevention of cerebrovascular disease (CVD) and is having minor dental or dermatologic procedure, or cataract surgery	Continue aspirin
On aspirin with moderate to high risk for cardiovascular events and requires non-cardiac surgery	Continue aspirin
On aspirin with low risk for cardiovascular events and requires non-cardiac surgery	Stop aspirin 7-10 days before procedure
On aspirin and requires coronary artery bypass grafting (CABG) surgery	Continue aspirin
On dual antiplatelet drug therapy and requires CABG surgery	Continue aspirin; Stop clopidogrel or ticagrelor 5 days before sugery; Stop prasugrel 7 days before surgery
On dual antiplatelet drug therapy and requires surgery within 6 weeks of bare-metal stent or within 6 months of drug-eluting stent and cannot wait the suggested time periods before surgery.	Continue dual antiplatelet drug therapy if surgery cannot be deferred until after those time periods (6 weeks for bare-metal stent/6 months for drug-eluting stent).

References

1. Douketis JD, Spyropoulos AC, Spencer FA, et al. "Perioperative management of antithrombotic therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines." *Chest.* 2012;141(2 SUPPL.):e326S-e350S.
2. Spyropoulos AC, Douketis JD. "How I Treat Anticoagulated Patients Underoing an Elective Procedure or Surgery." *Blood*. 2012;DOI 10.1182/blood-2012-06-415943.
3. Baron TH, Kamath PS, McBane RD. "Management of Antithrombotic Therapy in Patients Undergoing Invasive Procedures." *NEJM* 2013;368:2113-24.
4. Tun NM, Oo TH. "Prevention and treatment of venous thromboembolism with new oral anticoagulants: a practical update for clinicians." *Thrombosis.* 2013;2013:183616

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Management of Anticoagulation in the Peri-Procedural Period

A TOOL FOR CLINICIANS

Despite the considerable efficacy of antithrombotics and the increased number of oral anticoagulants now available, preventable bleeding and thrombotic events are still unacceptably common. While recently marketed agents require less laboratory monitoring, problems with the clinical management of anticoagulated patients persist, particularly in the peri-procedural period.

Surgery and invasive medical interventions increase the risk of bleeding, while withholding anticoagulants increases the risk of thrombosis due to the underlying condition(s) for which anticoagulation was originally prescribed. The clinical team must therefore balance these competing risks and make educated decisions regarding the decision to interrupt oral anticoagulation for a medical procedure and, if interrupted, whether to "bridge" anticoagulation with injectable anticoagulants, such as low molecular weight heparin (LMWH) in warfarin treated patients.

This guide is intended to:

- Assist clinicians in the simultaneous evaluation of procedure-related bleeding risk and underlying risk of thrombosis
- Guide decisions regarding the interruption of anticoagulation and the use of anticoagulant "bridging"
- Provide detailed guidance for drug dosing and laboratory monitoring in the peri-procedural period
- Encourage clear communication between clinicians involved in prescribing anticoagulants and performing invasive procedures

This material was created in April 2014 by the multidisciplinary members of the Peri-Procedural Task Force of the New York State Anticoagulation Coalition and IPRO, the Medicare Quality Improvement Organization for New York State, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the U.S. Department of Health and Human Services. The contents do not necessarily reflect CMS policy. 10SOW-NY-AIM7.3-14-01

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Table 1: RISK ASSESSMENT[1,2]

INSTRUCTIONS

1. Perform patient anticoagulation assessment 7+ days prior to procedures.
2. Categorize procedure-related bleeding risk using columns to right.
3. Categorize underlying thrombosis risk using rows below.
4. View suggestions for anticoagulant interruption and bridging in cell where row and column intersect.
5. View specific guidance for novel oral anticoagulant (NOAC) users in Table 2.
6. View specific guidance for warfarin users in Table 3.
7. View specific guidance for antiplatelet users in Table 4.

DISCLAIMER: Anticoagulation prescribing is highly complex, and should be conducted with the greatest care on a case by case basis, considering the complete patient medical profile. The information presented is for general guidance only. Prescribers are encouraged to consult the most current medical evidence and organizational policies and procedures.

HIGH BLEEDING RISK PROCEDURES (2 day risk of major bleed ≥ 2%)	LOW BLEEDING RISK PROCEDURES (2 day risk of major bleed <2%)	MINIMAL BLEEDING RISK PROCEDURES
Major surgery with extensive tissue injury ■ Cancer surgery ■ Major orthopedic surgery ■ Reconstructive plastic surgery ***Urologic or Gastrointestinal surgery*** ■ Transurethral prostate resection, bladder resection or tumor ablation ■ Nephrectomy, kidney biopsy ■ Colonic polyp resection ■ Bowel resection ■ Percutaneous endoscopic gastrotomy (PEG) placement, endoscopic retrograde cholangiopancreatography (ERCP) ***Other*** ■ Cardiac, intracranial, or spinal surgery ■ Surgery in highly vascular organs (kidneys, liver, spleen) ■ Multiple tooth extractions ■ Any major operation (procedure duration >45 minutes) ■ Pacemaker or cardioverter-defibrillator device implantation*	■ Minor dental procedures (simple dental extractions, restorations, prosthetics, endodontics) ■ Cutaneous/lymph node biopsies ■ Shoulder/foot/hand surgery ■ Coronary angiography ■ Gastrointestinal endoscopy +/- biopsy ■ Colonoscopy +/- biopsy ■ Abdominal hysterectomy ■ Laparoscopic cholecystectomy ■ Abdominal hernia repair ■ Hemorrhoidal surgery ■ Bronchoscopy +/- biopsy ■ Epidural injections with INR <1.2 ■ Pacemaker battery change ■ Arthroscopy	■ Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) ■ Cataract procedures ■ Dental cleanings, fillings

UNDERLYING THROMBOEMBOLIC RISK	A	B	C
(>10%/yr. risk of arterial thromboembolism [ATE] or >10%/month risk of venous thromboembolism [VTE]) • Any mechanical mitral valve • Caged ball or tilting disc valve in mitral/aortic position • Stroke or transient ischemic attack (TIA) within last 6 months in patients with a mechanical valve • Atrial fibrilliation (AF) with $CHADS_2$ score of 5 or 6 • Stroke or TIA within past 3 months in patients with AF • Rheumatic valvular heart disease • VTE within past 3 months • Severe thrombophilia • Deficiency of protein C, protein S or antithrombin • Antiphospholipid antibodies • Multiple thrombophilias **1 HIGH**	**NOAC users:** Interrupt NOAC. Bridging with low molecular weight heparin (LMWH) not suggested for NOACs (See Table 2); **Warfarin users:** Interrupt warfarin and bridge with LMWH suggested (See Table 3)† A1	**NOAC users:** Consider interrupting NOAC using clinical judgment. Bridging with LMWH not suggested for NOACs (See table 2); **Warfarin users:** Consider interrupting warfarin using clinical judgment. Bridging with LMWH suggested if warfarin interrupted (See table 3) B1	Do not interrupt anticoagulants. C1
(4–10%/yr. risk of ATE or 4–10%/month risk of VTE) • Bileaflet aortic valve replacement (AVR) WITH major risk factors for stroke • AF with $CHADS_2$ score of 3 or 4 • VTE within past 3-12 months • Recurrent VTE • Non-severe thrombophilia • Active cancer **2 MEDIUM**	**NOAC users:** Interrupt NOAC. Bridging with LMWH not suggested for NOACs (See Table 2); **Warfarin users:** Interrupt warfarin and consider bridging with LMWH (See Table 3) A2	**NOAC users:** Consider interrupting NOAC using clinical judgment. Bridging with LMWH not suggested for NOACs (See table 2); **Warfarin users:** Consider interrupting warfarin with or without LMWH bridging based on clinician judgment (See Table 3) B2	Do not interrupt anticoagulants. C2
(<4%/yr. risk of ATE or <4%/mos. risk of VTE) • Bileaflet AVR WITHOUT major risk factors for stroke • AF with $CHADS_2$ score of 0–2 (and no prior stroke or TIA) • VTE more than 12 months ago **3 LOW**	**NOAC users:** Interrupt NOAC. Bridging with LMWH not suggested for NOACs (See Table 2); **Warfarin users:** Interrupt warfarin. Bridging with LMWH not necessary (See Table 3) A3	**NOAC users:** Interrupt NOAC, Bridging with LMWH not suggested for NOACS (See Table 2); **Warfarin users:** Interrupt warfarin. Bridging with LMWH not necessary (See Table 3) B3	Do not interrupt anticoagulants. C3

Table 2: NOVEL ORAL ANTICOAGULANT (NOAC) INTERRUPTION SUGGESTIONS[1,4]

Drug‡	Patient§ Renal Function	Low Bleeding Risk Surgery** (2 or 3 drug half-lives between last dose and surgery)	High Bleeding Risk Surgery†† (4 or 5 drug half-lives between last dose and surgery)	Resumption of Therapy: Low Bleeding Risk Surgery	Resumption of Therapy: High Bleeding Risk Surgery
Dabigatran					
t ½ = 14–17 hrs	CrCl > 50 mL/min	Last dose: 2 days before procedure	Last dose: 3 days before procedure	Resume on day after procedure (24 h postoperative)	Resume 2-3 days after procedure (48-72 h postoperative)‡‡
t ½ = 16–18 hrs	CrCl 30–50 mL/min	Last dose: 3 days before procedure	Last dose: 4–5 days before procedure		
Rivaroxaban					
t ½ = 8–9 hrs	CrCl > 50 mL/min	Last dose: 2 days before procedure	Last dose: 3 days before procedure	Resume on day after procedure (24 h postoperative)	Resume 2-3 days after procedure (48-72 h postoperative)‡‡
t ½ = 9 hrs	CrCl 30–50 mL/min	Last dose: 2 days before procedure	Last dose: 3 days before procedure		
t ½ = 9–10 hrs	CrCl 15–29.9 mL/min§§	Last dose: 3 days before procedure	Last dose: 4 days before procedure		
Apixaban					
t ½ = 7–8hrs	CrCl >50 mL/min	Last dose: 2 days before procedure	Last dose: 3 days before procedure	Resume on day after procedure (24 h postoperative)	Resume 2-3 days after procedure (48–72 h postoperative)‡‡
t ½ = 17–18 hrs	CrCl 30–50 mL/min	Last dose: 3 days before procedure	Last dose: 4 days before procedure		
Edoxaban t ½ = 6–11 hrs	CrCl >50mL/min	Last dose: 2 days before procedure	Last dose: 3 days before procedure	Resume on day after procedure (24 h postoperative)	Resume 2-3 days after procedure (48–72 h postoperative)

The table above consists of the three NOACs currently available in the US and edoxaban (available in the UK, currently under FDA review in the US). As new medications become available, this list will be modified to include the latest available medications. In the patient with decreased renal clearance, allowance should be made for lower dosing and/or increased time between cessation of medication prior to the procedure to minimize increased bleeding risk.

* Recent evidence suggests that interruption of anticoagulation for ICD and pacemaker-related procedures is not necessary. See Birnie DH et al. *NEJM* 368(22):2084-2093.

† Therapeutic LMWH regimens include enoxaparin 1.5 mg/kg once daily or 1.0 mg/kg twice daily subcutaneously; dalteparin 200 IU/kg once daily or 100 IU/kg twice daily subcutaneously. Intermediate dose LMWH (i.e., enoxaparin 40 mg twice daily subcutaneously) has been less studied in this setting.

‡ Estimated t1/2 based on renal clearance.

§ CrCl calculated using Cockcroft-Gault method.

** Aiming for mild to moderate residual anticoagulant effect at surgery (12%–25%).

†† Aiming for no or minimal residual anticoagulant effect (3%–6%) at surgery.

‡‡ For patients at high risk for thromboembolism and high bleeding risk after surgery, consider administering a reduced dose of dabigatran (75 mg twice daily), rivaroxaban (10 mg once daily), or apixaban (2.5 mg twice daily) on the evening after surgery and on the following day (first postoperative day) after surgery.

§§ Value for patients receiving rivaroxaban, 15 mg once daily.