**Appendix 3. Antithrombotics**

Antithrombotics include medications classified as anticoagulants or antiplatelet agents (APAs). Anticoagulants prevent the clotting of blood by interfering with the native clotting cascade and include the following 4 drug classes: vitamin K antagonists (eg, warfarin), heparin derivatives (eg, unfractionated [UFH] and low molecular weight [LMWH], fondaparinux [Arixtra, GlaxoSmithKline, Research Triangle Park, NC, USA]), direct factor Xa inhibitors (eg, ri- varoxaban [Xarelto, Janssen Pharmaceuticals, Inc, Raritan, NJ, USA], apixaban [Eliquis, Bristol-Myers Squibb Company, Princeton, NJ, USA], edoxaban [Savaysa, Daiichi Sankyo Co, LTD, Tokyo, Japan]), and direct thrombin inhibitors (eg, dabigatran [Pradaxa, Boehringer Ingelheim Pharmaceu- ticals Inc, Ridgefield, Conn, USA], hirudins, argatraban [Acova, Abbott Laboratories, North Chicago, Ill, USA]). APAs decrease platelet aggregation, thus preventing thrombus formation. APAs include the thienopyridines (eg, clopidogrel, [Plavix, Bristol-Myers Squibb/Sanofi Pharmaceu- ticals Partnership, Bridgewater, NJ, USA], prasugrel [Effient, Eli Lilly and Company, Indianapolis, Ind, USA], ticlopidine [Ticlid, Roche Pharmaceuticals, Nutley, NJ, USA], and ticagre- lor [Brilinta, AstraZeneca, Wilmington, Del, USA]), the protease-activated receptor-1 (PAR-1) inhibitor vorapaxar (Zontivity, Merck Sharp & Dohme Corp, Whitehouse Station, NJ, USA), glycoprotein IIb/IIIa receptor inhibitors (GPIIb/IIIa inhibitors) (eg, abciximab [ReoPro, Eli Lilly and Company, In- dianapolis, Ind, USA], eptifibatide [Integrilin, Merck Sharp & Dohme Corp, Whitehouse Station, NJ, USA], and tirofiban [Aggrastat, Medicure Pharma, Inc, Somerset, NJ, USA]),

**Patients on Antithrombotics**

Antithrombotic therapy is a well known risk factor for post-polypectomy bleeding, and can increase the procedure related risk by 3-5 fold. Antithrombotics include medications classified as anticoagulants or antiplatelet agents (Appendix 2). Current society guidelines recommend temporary cessation of antithrombotics prior to polypectomy. Importantly, the probability of a thromboembolic event related to the temporary interruption of antithrombotic therapy for an endoscopic procedure has been reported to be up to 3%, depending on the indication for antithrombotic therapy and individual patient characteristics. As a corollary, post polypectomy bleeding rates are highest in patients on antithrombotic bridge thereapy.[199-202] Thus, the peri-procedure management of patients on antithrombotics can be complex, including

considerations on dose adjustment, length of interruption, and the need for bridge therapy based on cerebrovascular accident risk prediction scores, such as the CHADSx-VASc index.

Recent meta-analysis supports the discontinuation of warfarin[203] and clopidogrel[203,204] in the peri-procedure period to prevent post polypectomy bleeding, demonstrating higher post polypectomy bleeding rates in the patients who continue therapy. Another study, not included in the meta-analysis, also showed a significantly higher percentage of patients who continue theinopyridine therapy during colonoscopy with polypectomy develop clinically important delayed post polypectomy bleeding than patients who discontinued therapy, the event rate was low (2.4%) and all post post polypectomy bleeds resolved without sequelae.[205] Guidance on the peri-procedure management of the new oral anticoagulants, including the direct thrombin inhibitor dabigatran and the direct factor Xa inhibitors (eg, rivaroxaban, apixaban, edoxaban), is lacking due to the paucity of evidence. They have distinct pharmokinetics, including a relatively short time to maximal effect from 1 to 4 hours, a half-life ranging from 8 to 15 hours, and variable excretion by the kidneys. Thus, to minimize the risk of post polypectomy bleeding in patients on these therapies, it is currently suggested that such agents be stopped for at least 2 half-lives, with further adjustment appropriate in the setting of renal impairment.[206]

Recently, the removal of lesions up to 10mm with the use cold snare polypectomy has been shown to be safe in patients receiving anticoagulation with warfarin, even without prophylactic clipping. Delayed bleeding requiring hemostasis occurred less commonly after cold snare polypectomy than conventional polypectomy despite continuation of anticoagulants (0% vs 14%, P =0.027).[60] This is particularly relevant given the majority of lesions found during routine colonoscopy are less than 10mm.

Specific guidelines are lacking regarding antithrombotic management following large colorectal lesion resection. Such patients currently receive individualized assessment, balancing the risks of interrupting anticoagulation for colonoscopic polypectomy or mucosal resection against the risks of significant bleeding during and after the procedure. Further safety and outcomes data following polypectomy is necessary to better inform optimal timing of drug interruption and reinitiation.