Residency Review

WESTERN NEW ENGLAND UNIVERSITY
COLLEGE of PHARMACY

To Dual or Not to Dual?

By Amanda Pelland, PharmD
PGY-1 Western New England University
Pharmacy Practice Resident

Recommendations in antiplatelet and dual antiplatelet therapies (DAPT) continue to change. This leaves many providers with questions regarding appropriate therapy for their patients. Determining the appropriate agent and length of therapy is vital, due to the associated risks and benefits.

Low-dose aspirin is indicated in the majority of cases for secondary prevention for cardiovascular disease. Primary prevention is more of a challenge to determine when to initiate therapy. However, with the transition from the Framingham Risk Calculator to the 10-Year Heart Risk Calculator, the risk factors of age, gender, race, cholesterol, blood pressure, diabetes diagnosis, and smoking status are taken into account. This calculator was published in the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk and has been updated to incorporate the JNC-8 and USPSTF guidelines; it also assumes that the patient has no atherosclerotic cardiovascular disease (ASCVD). A 10-year risk is calculated and a recommendation for aspirin therapy is deduced when the score is >10%. It is important to always weigh the risk vs. benefit for your individual patient when determining whether or not to add aspirin therapy. Currently, there is no evidence supporting the use of 325mg of aspirin daily; 81mg is the recommended dose for daily aspirin therapy, due to the associated risks of high-dose aspirin therapy.

10-Year Heart Risk Calculator: www.cvriskcalculator.com

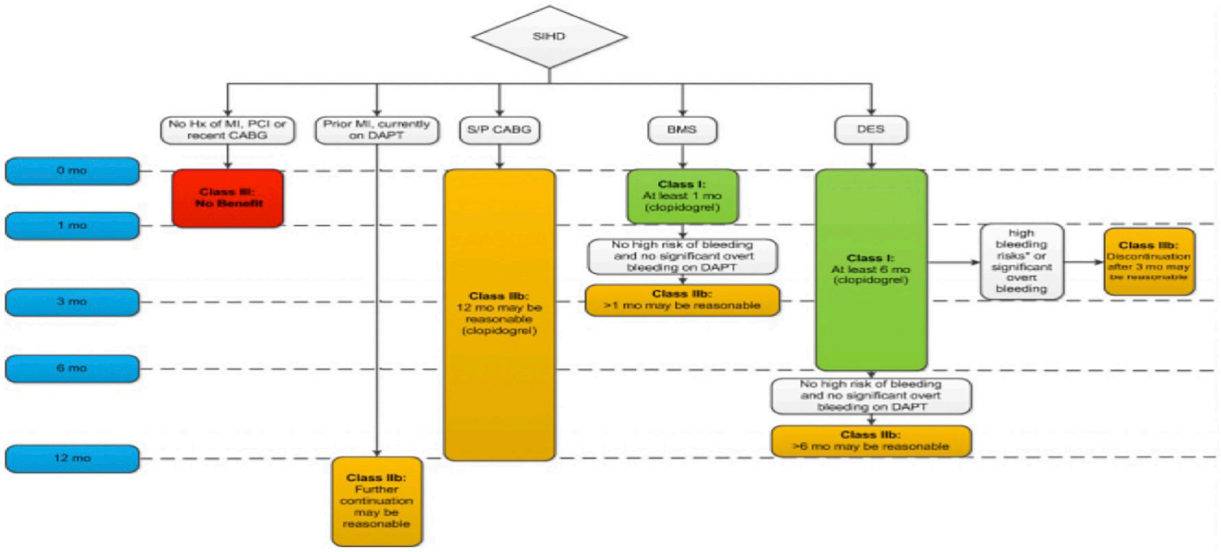
DAPT guidelines have been recently updated in March of 2016 by the American College of Cardiology and the American Heart Association task force. Recommendations were made based on appropriateness of DAPT as well as length of therapy. The major changes include the following:

- Patients with stable ischemic heart disease (IHD) who received a drug-eluting stent only need to receive DAPT for 6 months rather than the 12 months recommended in the guidelines, and they state -3 months may be appropriate if there is a high bleeding risk.[1]
- Patients after receiving a coronary artery bypass graft or a heart stent and bypass, acute coronary syndrome (ACS), may be reinitiated on DAPT.[1]
- Patients who have had a heart attack may benefit from 12 months of DAPT, unless there is an increased risk of bleeding, in which case 6 months of DAPT would be appropriate.[1]
- The recommendation of the initiation of low-dose 81mg aspirin daily has been strengthened and recommended to be continued indefinitely in those patients using DAPT.[1]

References:

1. American Heart Association News. New Guidelines Say Blood-Thinning Therapy Should Be Longer For Some, Shorter For Others [Internet]. American Heart Association; 2016 Mar 29 [cited 2016 May 5]. Available from: http://news.heart.org/new-guidelines-say-blood-thinning-therapy-should-be-longer-for-some-shorter-for-others/
2. Levine, GN, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease [Internet]. American College of Cardiology/American Heart Association; 2016 [cited 2016 April 27]. Available from: http://circ.ahajournals.org/content/early/2016/03/28/CIR.0000000000000404.full.pdf

Treatment Algorithm for Duration of P2Y12 Inhibitor Therapy in Patients With Stable Ischemic Heart Disease (SIHD) (Without ACS Within the Past Several Years)[2]:



Round One: Warfarin vs Novel Oral Anticoagulants (NOACs)

By Irini Salama, PharmD
PGY-1 Western New England University
Pharmacy Practice Resident

There are currently several options available for oral anticoagulation. Newer oral agents have been developed to target different stages of the coagulation cascade such as thrombin and factor Xa. These agents are compared to warfarin (Coumadin®), which is a vitamin K antagonist. NOACs require individualized dosing based on indication, as well as patient specific factors such as kidney function, age, and body weight (Table 1). It is important to note each of these factors, and to be aware of the risks and benefits when choosing oral anticoagulation therapy.

Warfarin has a narrow therapeutic window that is affected by several factors including genetic variations, drug interactions, and food interactions. Warfarin requires frequent monitoring of the International Normalized Ratio (INR) to evaluate efficacy, with the goal ranges based on the patient's indication for therapy. Clinical experience with warfarin is extensive and has been shown to be highly effective in reducing the risk of venous and arterial thromboemboli. Warfarin is the preferred oral agent in patients with heart valves; the other oral anticoagulant agents should not be used in those patients with heart valves.[1,2]

Direct thrombin inhibitors inactivate circulating and clot-bound thrombin (factor IIa). Currently dabigatran (Pradaxa®) is the only oral direct thrombin inhibitor. Dabigatran is indicated for the prevention and management of venous thromboembolic disease, and in stroke prevention in patients with atrial fibrillation. The dosing of dabigatran depends on the patient's clinical indication and renal function. Unlike warfarin, dabigatran does not require monitoring for efficacy.[1,2] In October 2015, the Food and Drug Administration granted accelerated approval to idarucizumab (Praxbind®) for use in patients who are taking dabigatran when there is a need to reverse the blood-thinning effects for life threatening or uncontrolled bleeding or when emergency surgery or procedures are required. This makes dabigatran the only NOAC with a known effective reversal agent at this time.[3]

Direct factor Xa inhibitors inactivate circulating and clot-bound Xa. Oral Xa inhibitors include rivaroxaban (Xarelto®), apixaban (Eliquis®), and edoxaban (Savaysa®). Like dabigatran, the dosing of these agents is dependent on several patient factors and do not require monitoring for efficacy. Currently, there is no available reversal agent. All three agents are indicated to reduce the risk of stroke or systemic emboli in nonvalvular atrial fibrillation and for the treatment of DVT/PE. Apixaban and rivaroxaban are also indicated for DVT prophylaxis after hip and knee replacement.[1,2]

Although NOACs are perceived as more convenient than warfarin due to the lack of monitoring for efficacy, and have fewer drug-drug and drug-food interactions, the factors such as renal function and affordability must be considered. NOACs are dose adjusted based creatinine clearance and are only available as brand name. Patient adherence is critical given that there is no lab monitoring. Ensuring a patient can afford the medication is imperative to assessing adherence. Clinical trials have proven that individually, the NOACs are at least as effective as warfarin for prevention of stroke and systemic embolism in patients with atrial fibrillation.

Table 1: Novel Oral Anticoagulants [1,2]

Drug Name	Non-Valvular AFib	DVT/PE Treatment	DVT Prophylaxis	Reduction in Risk of Recurrence of DVT/PE
Rivaroxaban[4]	**CrCl >50mL/min:** 20mg daily with evening meal **CrCl 15-50 mL/min:** 15mg daily with evening meal **CrCl <15 mL/min:** Avoid use	15mg BID with food for 21 days, then 20mg daily with food **CrCl <30 mL/min:** Avoid use	10mg daily (for 12 days after knee replacement and 35 days after hip surgery) give 1st dose 6-10 hours after surgery. **CrCl ≤30mL/min**: Avoid use	20mg daily with food **CrCl <30ml/min:** Avoid use
Apixaban[5]	5mg BID unless the patient has two of the following: age ≥ 80 years, ≤ 60 kg, SCr ≥1.5 mg/dL, then give 2.5mg BID	10mg BID x 7 days then 5mg BID **CrCl <25 mL/min:** no recommendations	2.5mg BID (for 12 days after knee replacement and 35 days after hip surgery) give 1st dose 12-24 hours after surgery. **CrCl ≤30 mL/min:** no recommendations	2.5mg BID after at least 6 months of treatment doses for DVT or PE.
Edoxaban[6]	**CrCl > 95 mL/min:** DO NOT USE **CrCl 51-95 mL/min:** 60mg daily **CrCl 15-50 mL/min:** 30mg daily **CrCl <15ml/min:** Avoid use	60mg daily after 5-10 days of treatment with a parenteral anticoagulant **CrCl 15-50 mL/min or body weight ≤ 60 kg:** 30mg daily **CrCl ≤ 15 mL/min:** Avoid use		
Dabigatran[7]	**CrCl > 30 mL/min:**150mg BID **CrCl 15-30 mL/min:** 75mg BID **CrCl <15 mL/min:** Avoid use	150mg BID start after 5-10 day of parenteral anticoagulation **CrCl ≤30 mL/min:** no recommendations	**CrCl >30 mL/min*:**110mg on day one, then 220mg daily **CrCl ≤30 mL/min*:** no recommendations.	

* Following hip replacement surgery

References:

1. Guyatt, G. H., Akl, E. A., Crowther, M., Gutterman, D. D., Schuünemann, H. J., & for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. (2012). Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 141(2), 7S–47S. http://doi.org/10.1378/chest.1412S3
2. Direct Oral Anticoagulants [Internet]. UpToDate, Waltham, MA; 2016 [cited 2016 May 7]. Available from: http://0-www.uptodate.com.wildpac.wne.edu/contents/direct-oral-anticoagulants-dosing-and-adverse-effects?source=machineLearning
3. FDA approves Praxbind, the first reversal agent for the anticoagulant Pradaxa [Internet] U.S. Food and Drug Administration 2015 [cited 2016, May 7]. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm467300.htm
4. Rivaroxaban [package insert on the internet]. Puerto Rico (PR): Janssen Ortho, LLC; 2011 [cited 2016 May 16]. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/202439s001lbl.pdf
5. Apixaban [package insert on the internet]. New Jersey (NJ): Bristol-Myers Squibb Company Princeton; 2015 [cited 2016, May 16]. Available from: http://packageinserts.bms.com/pi/pi_eliquis.pdf
6. Edoxaban [package insert on the internet]. New Jersey (NJ): Daiichi Sankyo Co., LTD; 2015 {cited 2016, May 16]. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206316lbl.pdf
7. Dabigatran [package insert on the internet]. Connecticut (CT): Boehringer Ingelheim Pharmaceuticals, Inc; 2015 [cited 2016, May 16]. Available from: http://docs.boehringeringelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf