Objectives:

The purpose of these inpatient care guidelines is to provide an evidence-based blueprint for the acute care of patients with atrial fibrillation (AF) and atrial flutter (AFL) at the University of Alabama Birmingham. It is hoped that this standardization of care will result in improved patient outcomes, shorter length of ICU/hospital stay, standardization of cardiology consultation, and overall cost savings for the system. This document will discuss recommendations for electrical cardioversion of unstable patients with AF/AFL, pharmacologic cardioversion of AF and AFL (as well as contraindications), and management of anticoagulation.

Incidence:

Atrial fibrillation (AF) and atrial flutter (AFL) are the most common sustained arrhythmias in the U.S., affecting 2.5 million adults with the majority of patients over the age of 65. AF/AFL is associated with numerous comorbidities including hypertension, coronary artery disease, heart failure, and valvular heart disease. The cost of direct care of patients with AF in the U.S. is an estimated $6.65 billion annually, the majority of which is attributed to hospitalizations due to rapid ventricular response, heart failure, and stroke. New onset Atrial Fibrillation is seen in critically ill patients with variable frequency, from 4 to 15% in a surgical ICU. The underlying pathophysiology and etiology of AF during critical illness differs from that of non-critically ill patients due to the potential for reversible factors including inflammation, electrolyte disturbance, adrenergic overstimulation, myocardial stretch, inappropriate oxygen delivery to the myocardium, and the use of proarrhythmic drugs.

Summary of Recommendations:

Atrial fibrillation is a common postoperative arrhythmia and can represent a major source of morbidity and mortality. Treatment of atrial fibrillation is directed at three main objectives: controlling the ventricular response, preventing thromboembolism, and maintaining sinus rhythm. Therapeutic decisions also hinge on patients’ hemodynamic stability. In patients who are hemodynamically unstable, direct current cardioversion is the first line therapy and pharmacotherapy should be used as adjunctive treatment. In patients who are hemodynamically stable, pharmacologic treatment including class I (beta-blockers), class III (amiodarone), or class IV (nondihydropyridine calcium channel blockers) agents are viable options.

In the setting of normotension and grossly intact systolic function (EF>35%) beta blockade should be utilized first line. Beta blockade is superior to calcium channel blockers (AFFIRM trial: 70% control with BB vs 54% control with CCB) and thusly should be first line in those patients with grossly normal systolic function. If beta-blockade therapy is unsuccessful, then second line regimen should be chosen based on blood pressure (CCB vs amiodarone). If the patient is normotensive, then calcium channel blockers may be utilized. If the patient is relatively hypotensive (SBP <110mmhg) or has labile blood pressure, then calcium channel blockers should be avoided. In this setting, amiodarone should be utilized. CCB may be more effective than amiodarone in regards to 24hr rate control, but are associated with a higher incidence of hypotension (30%).

In the setting of patients with confirmed or suspected acute-onset gross systolic dysfunction, amiodarone should be utilized first line. If amiodarone bolus therapy is successful*, a drip or oral regimen should be started dependent upon the patient’s PO status. If a drip is initiated, it should be converted to oral
regimen when able, ideally after 24 hours. Oral therapy should be continued for one month to cover acute illness. Should amiodarone therapy be unsuccessful in the setting of acute-onset gross systolic dysfunction, cardiology consult should be obtained and digoxin therapy considered. Because of their negative inotropic effect, calcium channel antagonists may further decompensate patients with left ventricular systolic dysfunction and symptomatic heart failure. In the absence of gross systolic dysfunction (EF<35%) beta blockade and calcium channel blockers may be utilized.

When rate control is compared to rhythm control, they have equal outcomes in regards to mortality however rhythm control strategies lead to increased hospitalizations. Thusly, a rate control strategy generally should be the goal. However, a rhythm control strategy should be considered in the following patients: young (<65yo), first episode of AF, AF precipitated by acute illness/trauma. Also, those patients whom it is difficult to obtain rate control and those patients who have tachycardia mediated cardiomyopathy. It is the recommendation of this protocol in an acute setting of AF/AFL with RVR, to first establish rate control and then assess if the patient would benefit from further rhythm control, and a cardiology consult should be sought.

Clinical Practice Guideline

I. Diagnosis/Workup - For patients with tachycardia (>120bpm) and irregular rhythm concerning for atrial fibrillation:

1. EKG to confirm Atrial Fibrillation with Rapid Ventricular Rate, HR >120bpm
   a. Evaluate for accessory pathway (Figure 2a) and contraindications for pharmacologic management
2. Obtain CBC, BMP, Mg, Ph, TSH
   a. Optimize electrolytes
3. Obtain Troponin if ST changes on EKG or chest pain
   b. If evidence of rate-related ischemia obtain cardiology consult & follow cardioversion algorithm (Figure 1)
4. CXR & BNP to evaluate for volume overload
5. Echo to evaluate for structural heart disease and/or heart failure
   c. Consider POCUS to evaluate for gross assessment of EF
   d. If evidence of acute heart failure (pulmonary edema, respiratory distress, grossly diminished EF): cardiology consult & cardioversion algorithm (Figure 1)
6. Assess Blood Pressure
   e. Hypotension (SBP <90) – proceed with cardioversion algorithm (Figure 1)
      i. Transfer patient to ICU setting
   f. Normotension (SBP>90) – proceed with pharmacologic algorithm (Figure 2)
      i. Continuous telemetry, transfer to step down or ICU
      ii. Dosing to follow medication dosing (table 1)
Cardioversion algorithm
(Figure 1)

Evaluate etiology of hypotension

Primary

- Immediate direct current cardioversion. 200J synchronized (can increase up to 360J). BMI >30 = 360J synchronized

- Consider pre-procedural anticoagulation (if >48hours)*

- Successful Cardioversion

  - Consider post-cardioversion anticoagulation*

  - Ibutilide

- Unsuccessful Cardioversion

  - STAT Cardiology Consult

Secondary

- Treat underlying condition:
  - Sepsis
  - hypovolemia/hemorrhage
  - hypoxia/respiratory failure
  - ACS
  - PE

Primary hypotension – hypotension directly related to rapid ventricular rate
Secondary Hypotension – underlying condition leading to hypotension, exclusive of rapid ventricular rate
Successful cardioversion – return to sinus rhythm
*See anticoagulation algorithm
Step 1: Evaluate for Accessory Pathway
(Figure 2a)

Accessory Pathway\(^a\) {wide/polymorphic QRS, WPW, delta wave}

- **Yes**
  - EP Consult\(^4\)
- **No**
  - Proceed to Step 2

Consider procainamide or ibutilide\(^5\)

Defibrillator at bedside

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\(^{a}\)Wolff Parkinson White (WPW) - Hallmark ECG findings include short PR interval and prolonged QRS (> 0.12s) with an initial slurring upstroke ("delta" wave). If accessory pathway suspected or confirmed, consult cardiology/EP. Many anti-arrhythmic are contraindicated in the setting of an accessory pathway.

\(^4\) Many anti-arrhythmics are contraindicated in the setting of an accessory pathway. AV nodal blocking agents (BB, CCB, Digoxin) can be fatal – accelerates anterograde conduction through the accessory pathway to the extent that ventricular fibrillation occurs.

\(^5\) In the setting of an accessory pathway or pre-excitation syndrome Procainamide (50-100mg every 2-5 min to a max of 17mg/kg OR 1 gram, whichever is less) or ibutilide (0.01mg/kg max 1mg over 10 min) are the treatment of choice for chemical conversion.
Step 2: Evaluate for heart failure

(Figure 2b)

No Systolic Heart Failure (EF>40%)?

Beta Blocker

SBP > 100
Metoprolol IV, up to 3 doses

Success^  
PO beta blockade

SBP 90 -100 or labile''
Esmolol gtt titrated to a HR goal of 90-110

SBP >110
CCB: Diltiazem IV; may repeat x1, then start gtt

Consider AC^*

SBP <110
Amiodarone IV; may repeat x 1, then start gtt/PO~

Consider AC^*

SBP < 110

^ Successful pharmacologic management — HR <110bpm acutely. At DC, HR <110bpm for patients with preserved LV function\(^1\) or <80bpm for patients with diminished LV function\(^4\)

*See anticoagulation algorithm

~ Amiodarone gtt only required for ventricular arrhythmias. In the setting of AF/AFL okay to start PO after response to bolus if patient able.
Step 2: Evaluate for heart failure
(Figure 2c)

Known or concern for Systolic Heart Failure (EF<40%)

Chronic

Beta Blocker

SBP > 100
Metoprolol IV, up to 3 doses

Success

PO beta blockade
Consider AC

Failure

SBP 90-100 or labile
Esmolol gtt titrated to a HR goal of 90-110

Success

Amiodarone IV; may repeat x 1

Acute Onset

Amiodarone gtt
Consider AC
Oral conversion
Cardiology Consult

Success*

Failure

Consider Digoxin

# in those patients with a systolic blood pressure below 100 or with labile blood pressure consider utilization of esmolol given shorter half-life and ability to titrate.

*Successful pharmacologic management — HR <110bpm acutely. Prior to discharge a HR <110bpm for patients with preserved LV function17 or <80bpm for patients with diminished LV function14

*See anticoagulation algorithm
Step 3: Consider the appropriateness of a rhythm control strategy

After rate control is achieved acutely, a therapeutic goal of restoring normal sinus rhythm should be pursued for patients that meet all of the following criteria:

1. Young (<65yo)
2. First Episode of Atrial Fibrillation
3. Atrial Fibrillation precipitated by acute illness

Management of patients meeting above criteria:

1. If rhythm control was restored with medications above, continue medication (BB, CCB, Amio) and outpatient cardiology referral.
2. If rate control is achieved, but remains in atrial fibrillation, inpatient cardiology consult for rhythm control strategy.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Warnings/contraindications</th>
<th>IV Dosing</th>
<th>PO Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcium Channel Blockers</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Diltiazem</td>
<td>AV Nodal block</td>
<td>0.15-0.25mg/kg (10-20mg; max 25mg) IVP bolus over 2 min, consider 2nd bolus 15 minutes later. Start infusion at 5mg/hr, titrate by 2.5mg/hr every 30 min for maximum dose 15mg/hr [onset 2-7 min]</td>
<td>120-360mg daily divided doses</td>
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<td></td>
<td>Negative inotrope</td>
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<tr>
<td></td>
<td>CI: Systolic Heart Failure</td>
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<tr>
<td>Verapamil</td>
<td>Vasodilator</td>
<td>2.5 – 5mg IVP over 2 min, second dose of 5-10mg may be given 15-30 min after initial dose, max total dose 20-30mg [onset 3-10 min]</td>
<td>120 -360mg daily divided doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: Systolic Heart Failure</td>
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<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
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<tr>
<td>Metoprolol</td>
<td>AV Nodal block</td>
<td>5mg IVP every 5-20 min x 3 [onset 5 min]</td>
<td>If conversion after 5mg IV → 25mg PO BID. 10mg IV → 50mg PO BID. 15mg IV → 75 PO BID [onset 4-6 hours]</td>
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<tr>
<td></td>
<td>Caution with decompensated heart failure</td>
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<tr>
<td>Esmolol</td>
<td>AV Nodal block</td>
<td>50mcg/kg/min, titrated upward in 50mcg/kg/min Q5 min to max of 300mcg/kg/min [onset &lt;5min]</td>
<td></td>
<td>Short half-life, better for tenuous BP</td>
</tr>
<tr>
<td></td>
<td>Caution with decompensated heart failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
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<tr>
<td>Amiodarone</td>
<td>Pulmonary toxicity; Thyroid toxicity</td>
<td>150mg IV over 10 min, consider second dose for non-response. 1mg/min IV x 6 hours, 0.5mg/min IV x 18 hours</td>
<td>400 to 800 mg per day x 1 week; then 400 mg per day to complete one month of therapy.</td>
<td>Anti-arrhythmic Useful in pts with decompensated heart failure Gtt should be administered through midline or central access. Peripheral OK for bolus.</td>
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<tr>
<td>Digoxin</td>
<td>AV nodal block</td>
<td>IV loading: 8-12mcg/kg IBW, administer load in 3 doses as 50%, 25%, 25% Q.6 hours.</td>
<td>Loading dose: 10-15mcg/kg IBW, administer load in 3 doses as 50%, 25%, 25% Q.6 hours.</td>
<td>Therapeutic drug monitoring recommended to reduce risk of adverse events Steady state @ 5-7 days</td>
</tr>
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<td></td>
<td>Renal impairment increases the risk of drug accumulation</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: ESRD</td>
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<td></td>
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</tr>
</tbody>
</table>
9. Kimura BJ. Point-of-care cardiac ultrasound techniques in the physical examination: better at the bedside. Heart 2017
19. Hindricks, Gerhard et al. “2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC.” European heart journal vol. 42,5 (2021)
Anticoagulation Therapy Guideline

Introduction:
Regardless of the strategy of symptom control, every patient with AF/AFL needs to be evaluated for thromboembolic risk. Maintenance of anticoagulation in the immediate setting is critical to prevent systemic thromboembolism including stroke following pharmacologic or electrical cardioversion, which occurs within the first 3 days of restoration of sinus rhythm.1

I. Indications
    a. Elective cardioversion under cardiology guidance, no recommendations per this guideline.
    b. Cardioversion for Instability
       i. <48 hours
          1. No need for anticoagulation if <48 hours and CHA2DS2-VASc Low (see below)
       ii. >48hrs or unknown
          1. Anticoagulate as soon as possible, continue for 4 weeks.
          2. No need for pre-cardioversion TEE in the setting of instability.
    c. CHA2DS2-VASc (Appendix A)
       i. For patients with AF and an elevated CHA2DS2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended (see below).

II. Contraindications
    a. Absolute contraindications:
       i. Major active bleeding (bleeding requiring > 2 units PRBC transfusion, decrease in hemoglobin by ≥ 2 g/dL, or bleeding in a critical area or organ)
       ii. Platelets < 25 K/microliter
       iii. Spinal procedure and/or epidural placement
       iv. Severe uncontrolled malignant hypertension
    b. Relative contraindications:
       i. Brain metastases with higher risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer)
       ii. Intracranial or central nervous system (CNS) bleeding within the past 4 weeks
       iii. Recent high-risk surgery or bleeding event
       iv. Active but non-life threatening bleeding
       v. Active gastrointestinal (GI) ulceration at high risk of bleeding
       vi. Platelets < 50 K/microliter, consider consult to Benign Hematology

III. Assessing Bleeding Risk
    a. HAS-BLED 6 (Appendix B)
       i. ≥3 high risk of bleeding
          1. Correct modifiable factors
          2. If still ≥3, anticoagulation per attending discretion
             a. Consider lower dose DOAC
                i. In patients with atrial fibrillation, dabigatran given at a dose of 110 mg was associated with rates of stroke and
systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage\(^7\).

ii. HAS-BLED score > CHA\(_2\)DS\(_2\)-VASc
1. Correct modifiable factors
2. If still ≥3, anticoagulation per attending discretion
   a. Consider lower dose DOAC (see above - III.a.i.2.a.i.)

IV. Anticoagulation Therapy Options & Dosing (Table 1, Table 2)
a. First-Line, Acute
   i. Heparin
b. Second-Line, Acute
   i. Lovenox\(^8\)
      1. Enoxaparin is noninferior to UFH for prevention of ischemic and embolic events, bleeding complications, and death in TEE-guided cardioversion of atrial fibrillation. Its easier application and more stable anticoagulation may make it the preferred drug for initiation of anticoagulation in this setting\(^8\).
   c. First-Line, Oral
      i. Direct-acting Oral Anticoagulants (DOACs) (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in DOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve).
         1. For patients with diminished CrCl, discuss with pharmacy regarding reduced doses of direct thrombin or factor Xa inhibitors.
         2. Dabigatran, Rivaroxaban, Edoxaban are not recommended in ESRD
d. Second-Line, Oral
   i. Warfarin
e. Special Populations
   i. In patients with moderate – severe mitral stenosis or a mechanical heart valve, Warfarin is preferred.
   ii. Patients on DAPT for prior PCI
      1. Patients who require dual antiplatelet therapy for percutaneous coronary intervention (PCI) AND with AF at increased risk of stroke (based on above CHA\(_2\)DS\(_2\)-VASc) triple therapy (oral anticoagulant, aspirin, and P2Y12 inhibitor) should be prescribed
         a. Clopidogrel is preferred over prasugrel.
         b. Transition to double therapy (oral anticoagulant and P2Y12 inhibitor) at 4 to 6 weeks, per cardiology outpatient follow up
      2. In patients with AF at increased risk of stroke (based on CHA\(_2\)DS\(_2\)-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with P2Y12 inhibitors (clopidogrel) and low-dose rivaroxaban (15 mg daily) is reasonable to reduce the risk of bleeding as compared with triple therapy.
### Appendix A: CHA₂DS₂-VASc

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (prior MI, PAD, or aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65 to 74 y</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (ie, female sex)</td>
<td>1</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
</tr>
</tbody>
</table>

### Appendix B: HAS-BLED

<table>
<thead>
<tr>
<th>HAS-BLED</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (systolic blood pressure &gt;160 mm Hg)</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal renal and liver function* (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding tendency/predisposition*</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs (if on warfarin)*</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (eg, age &gt;65 y)</td>
<td>1</td>
</tr>
<tr>
<td>Drugs or alcohol (1 point each)*</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
</tr>
</tbody>
</table>
Figure 1: Anticoagulation Algorithm

Cardioversion
>48 hours after onset
OR Qualifying
CHA$_2$DS$_2$-VASc score

Review for absolute contraindications

HAS-BLED SCORE

<\(3\) or HAS-BLED<\(CHA_2DS_2-VASc\)

Full anticoagulation per protocol

\(\geq3\) or HAS-BLED>\(CHA_2DS_2-VASc\)

Correct modifiable factors

Consider lower-dose DOAC
<table>
<thead>
<tr>
<th>MOA</th>
<th>Drug</th>
<th>Warnings/contraindications</th>
<th>Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor Xa and thrombin inhibitor</td>
<td>Unfractionated Heparin</td>
<td>Contraindicated: History of heparin induced thrombocytopenia; Uncontrolled active bleeding</td>
<td>Use Powerplan: Heparin Infusion for Cardiac Indications: 70 units/kg bolus (optional); 15units/kg/hr titrated to anti-Xa 0.3-0.7</td>
<td>For patients with exposure to DOACs in the past 48-72 hours, select PTT titration option within the powerplan</td>
</tr>
<tr>
<td>Factor Xa inhibitor and mild thrombin inhibitor</td>
<td>Enoxaparin</td>
<td>Contraindicated: History of heparin induced thrombocytopenia; Uncontrolled active bleeding</td>
<td>1mg/kg SubQ BID CrCl: &lt;30mL/min 1mg/kg Daily</td>
<td>Requires dose adjustment for renal dysfunction;</td>
</tr>
<tr>
<td>Direct Thrombin Inhibitors</td>
<td>Bivalirudin</td>
<td>Contraindicated: Uncontrolled active bleeding;</td>
<td>0.15mg/kg/hr; CrCl 30-59 mL/min: 0.08 mg/kg/hr CrCl 10-29mL/min: 0.04mg/kg/hr IHD/CVVHDF: 0.07mg/kg/hr</td>
<td>Titrated to PTT 1.5-2.5x control For use in patients with HIT or history of HIT or ATIII deficiency with demonstrated heparin resistance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MOA</th>
<th>Drug</th>
<th>Warnings/contraindications</th>
<th>PO Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin K Antagonist</td>
<td>Warfarin</td>
<td>Contraindicated: Uncontrolled active bleeding; epidural analgesia; Pregnancy Warnings: dosing subject to major drug-drug and drug-food interactions</td>
<td>Initial dosing: 2.5–10 mg every 24 h titrated to range INR: 2.0–3.0; target of 2.5</td>
<td></td>
</tr>
<tr>
<td>Direct factor Xa Inhibitors</td>
<td>Rivaroxaban</td>
<td>Contraindicated: Uncontrolled active bleeding</td>
<td>CrCl &gt;50 mL/min: 20 mg once daily CrCl 15–50 mL/min: 15 mg once daily</td>
<td>No coagulation specific monitoring recommended</td>
</tr>
<tr>
<td></td>
<td>Apixaban</td>
<td>Contraindicated: Uncontrolled active bleeding</td>
<td>5 mg twice daily 2.5 mg twice daily in patients with at least two of: age &gt;80 years, body weight &lt;60 kg, serum creatinine &lt;1.5 mg/dL</td>
<td>Dose adjustments required for patients receiving concomitant ketoconazole, itraconazole, or ritonavir</td>
</tr>
<tr>
<td>Thrombin Inhibitor</td>
<td>Dabigatran</td>
<td>Contraindicated: Uncontrolled active bleeding; Mechanical prosthetic heart valve</td>
<td>CrCl &gt;30 mL/min: 150 mg twice daily CrCl 15–30 mL/min: 75 mg twice daily May consider 110mg BID dosing for patients with higher bleeding risk</td>
<td>Dose adjustments required for patients receiving concomitant ketoconazole or dronedarone</td>
</tr>
</tbody>
</table>
References

2. Lane, Deirdre A, and Gregory Y H Lip. “Use of the CHA(2)DS(2)-VASc and HAS-BLED scores to aid decision making for thromboprophylaxis in nonvalvular atrial fibrillation.” Circulation vol. 126,7 (2012);
5. Hindricks, Gerhard et al. “2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC.” European heart journal vol. 42,5 (2021):