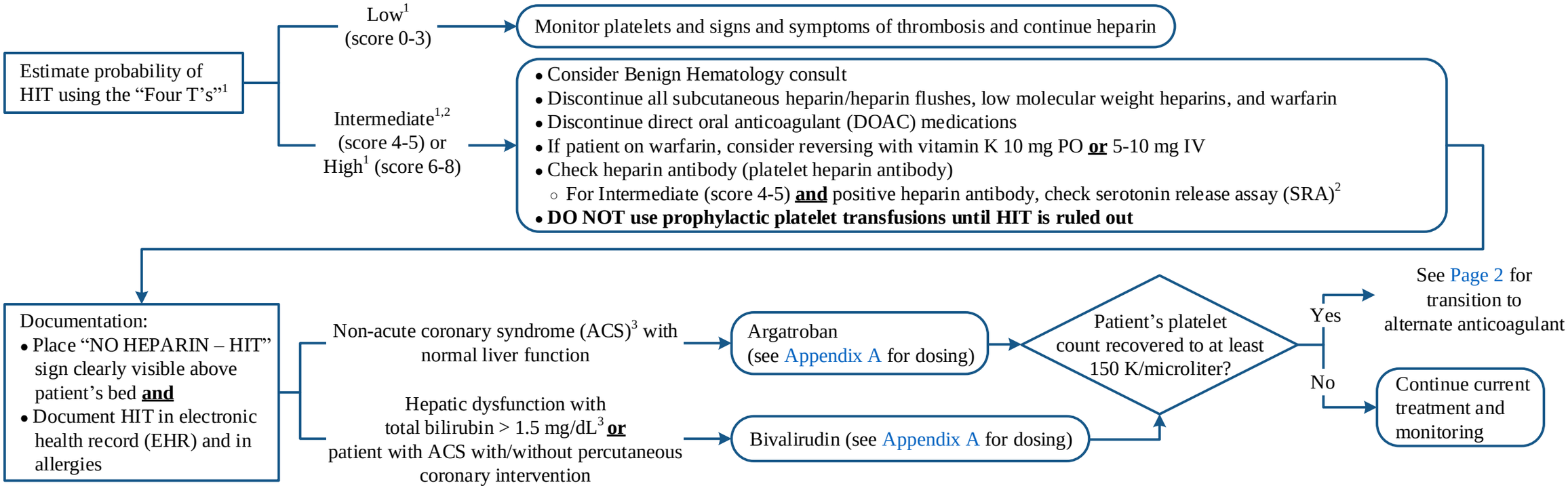
Heparin Induced Thrombocytopenia (HIT) Treatment



[1]**The Four T's** – add the values from each "T" category based on presence of criteria

	2	1	0
Thrombocytopenia	Platelet count fall > 50% **and** Nadir ≥ 20 K/microliter	Platelet count fall 30-50% (or platelet fall > 50% due to surgery), **or** Nadir 10-19 K/microliter	Platelet fall < 30% **or** Nadir < 10 K/microliter
Timing* of platelet fall onset	Onset between Days 5-10 **or** Platelet count fall than or equal to Day 1 with recent heparin (past 30 days)	Onset after Day 10 or timing unclear, **or** Platelet count fall less than or equal to Day 1 with recent heparin (past 31-100 days)	Platelet count fall less than Day 4 without recent heparin
Thrombosis or other sequelae	Proven new thrombosis **or** skin necrosis; or Acute anaphylactoid reaction after IV heparin bolus	Progressive **or** recurrent thrombosis; erythematous skin lesions, suspected thrombosis (not proven); asymptomatic upper-limb deep vein thrombosis (DVT)	None
O**T**her causes[4]	None evident	Possible	Definite

* First day of immunizing heparin exposure = Day 0

[2] In patients with a Four T score of Intermediate (4-5) **and** a positive heparin antibody, a negative SRA rules out HIT and a positive SRA confirms HIT

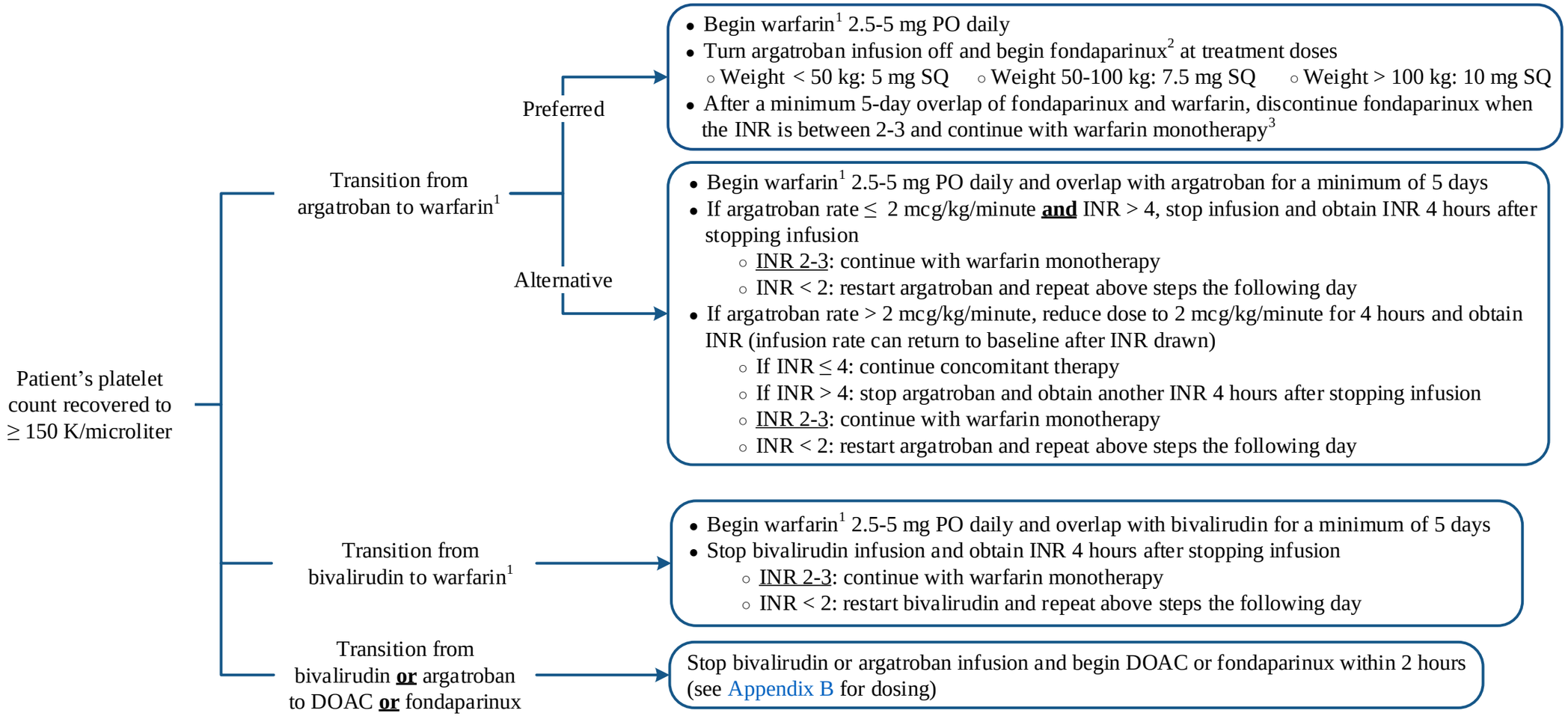
[3] Use of bivalirudin for non-ACS is not an FDA approved indication

[4] Examples of other causes include, but are not limited to: chemotherapy, drug-related, sepsis, disseminated intravascular coagulation (DIC)

Department of Clinical Effectiveness V9
Approved by the Executive Committee of Medical Staff on 02/18/2020

Heparin Induced Thrombocytopenia (HIT) Treatment

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*



[1] When initiating the transition to warfarin therapy DO NOT use a loading dose. The recommended maximum initial dose of warfarin is 5 mg. Overlap warfarin therapy with direct thrombin inhibitor (DTI) continuous infusion for at least 5 days.
[2] In patients with normal renal function (creatinine clearance > 50 mL/minute). Use caution in creatinine clearance 30-50 mL/minute and use is contraindicated in creatinine clearance < 30 mL/minute.
[3] Treat with warfarin for 4 weeks, unless there is an indication for long-term anticoagulation (e.g., active venous thromboembolism (VTE) or chronic atrial fibrillation)

APPENDIX A: Direct Thrombin Inhibitor (DTI) Dosing and Monitoring

DTI	Special dosing parameters	Dose	Monitoring	Notes and special considerations
Argatroban Plasma half-life = 39-51 minutes (in healthy subjects) Primarily hepatic elimination	Normal dosage	2 mcg/kg/minute	aPTT 2 hours after initiation and dose change	• Use of this medication causes **significant** elevation of PT/INR results due to interference with testing • Do not discontinue this medication based on an elevated INR value • Continue to monitor the patient for signs and symptoms of bleeding
	Consider dosage reduction with the following: • Child-Pugh[1] score > 6, • Total bilirubin > 1.5 mg/dL, • Heart failure • Multi-organ system failure • Severe anasarca • Status post cardiac surgery	0.5 mcg/kg/minute		
Bivalirudin Plasma half-life = 25 minutes (in healthy subjects) Metabolized by proteolytic cleavage with 20% renal elimination **Note:** Use of bivalirudin for non-ACS is not an FDA approved indication	Dose for HIT: Normal renal function Creatinine clearance < 30 mL/minute Patient on dialysis	0.15 mg/kg/hour 0.08 mg/kg/hour 0.02 mg/kg/hour	aPTT 2 hours after initiation and dose change	Use of this medication, causes mild elevation of PT/INR results due to interference with testing
	Dose for ACS with or without percutaneous coronary intervention: Normal renal function	Bolus dose 0.75 mg/kg, followed by 1.75 mg/kg/hour		
	Creatinine clearance < 30 mL/minute	Bolus dose 0.75 mg/kg, followed by 1 mg/kg/hour		
	Patient on dialysis	Bolus dose 0.75 mg/kg, followed by 0.25 mg/kg/hour		

[1] See Appendix C for Child-Pugh Scoring System

APPENDIX B: Non-heparin Anticoagulants Dosing and Monitoring

Drug	Mechanism of action	Primary mechanism of elimination	Dosing	Laboratory monitoring
Fondaparinux	Indirect factor Xa inhibitor	Renal (17-24 hours)	• Weight < 50 kg: 5 mg subcutaneously daily • Weight 50-100 kg: 7.5 mg subcutaneously daily • Weight > 100 kg: 10 mg subcutaneously daily	None
Apixaban	Direct factor Xa inhibitor	Hepatic (8-15 hours)	**Heparin induced thrombocytopenia with thrombosis (HITT):** • 10 mg PO twice daily for 1 week then, 5 mg PO twice daily **Isolated HIT:** • 5 mg PO twice daily until platelet recovery	None
Dabigatran	Direct factor Xa inhibitor	Renal (12-17 hours)	**HITT:** • 150 mg PO twice daily after ≥ 5 days of treatment with a parenteral non-heparin anticoagulant **Isolated HIT:** • 150 mg PO twice daily until platelet recovery	None
Rivaroxaban	Direct factor Xa inhibitor	Renal (5-9 hours)	**HITT:** • 15 mg PO twice daily for 3 weeks then, 20 mg PO daily thereafter **Isolated HIT:** • 15 mg PO twice daily until platelet recovery	None
Edoxaban	No information available, therefore no recommendation can be made			

Note:

- Considerations for transitioning to DOACs or fondaparinux:
  - **Only if patient is clinically stable (hemodynamic stability, no dialysis, no liver failure, non-surgical) and at average risk of bleeding**
  - **No data** exists for use in patients requiring dialysis
  - Not approved for treatment of acute HIT. Suggested dosing is extrapolated from venothromboembolism (VTE) trials and based on the limited published experience in HIT.
- The choice of agent maybe influenced by drug factors (cost, ability to monitor anticoagulants effects, route of administration, half-life, drug-drug interactions) and patient factors (kidney dysfunction, liver dysfunction, bleeding risk, clinical stability) and experience of the clinician

APPENDIX C: Child-Pugh Scoring System[1]

Chemical and biochemical parameters	Scores (points) for increasing abnormality		
	1	2	3
Encephalopathy	None	1 - 2	3 - 4
Ascites	None	Slight	Moderate
Albumin	> 3.5 g/dL	2.8 - 3.5 g/dL	< 2.8 g/dL
Bilirubin In primary biliary cirrhosis	< 2 mg/dL 1 - 4 mg/dL	2 - 3 mg/dL 4 -10 mg/dL	> 3 md/dL > 10 mg/dL
Prothrombin time prolonged **or** INR	1 - 4 seconds < 1.7	4 - 6 seconds 1.7 - 2.3	> 6 seconds > 2.3

[1] Child-Pugh score is obtained by adding the score for each parameter
Child-Pugh class:
Class A = 5 to 6 points
Class B = 7 to 9 points
Class C = 10 to 15 points

SUGGESTED READINGS

Cuker, A., Arepally, G. M., Chong, B. H., Cines, D. B., Greinacher, A., Gruel, Y., . . . Santesso, N. (2018). American Society of Hematology 2018 guidelines for management of venous thromboembolism: Heparin-induced thrombocytopenia. *Blood Advances*, *2*(22), 3360-3392. doi:10.1182/bloodadvances.2018024489

Greinacher, A. (2015). Heparin-induced thrombocytopenia. *New England Journal of Medicine*, *373*(3), 252-261. doi:10.1056/NEJMcp1411910

Kelton, J. G., Arnold, D. M., & Bates, S. M. (2013). Nonheparin anticoagulants for heparin-induced thrombocytopenia. *New England Journal of Medicine*, *368*(8), 737-744. doi:10.1056/NEJMct1206642

Linkins, L. A., Dans, A. L., Moores, L. K., Bona, R., Davidson, B. L., Schulman, S., & Crowther, M. (2012). Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*, *141*(2 Suppl), e495S-e530S. doi:10.1378/chest.11-2303

Pugh, R., Murray-Lyon, I. M., Dawson, J. L., Pietroni, M. C., & Williams, R. (1973). Transection of the oesophagus for bleeding oesophageal varices. *British Journal of Surgery*, *60*(8), 646-649. doi:10.1002/bjs.1800600817

DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the anticoagulant experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

Parvaneh Erfan, BS, AS (Core Lab)
Shuwei Gao, MD (General Internal Medicine)
Wendy Garcia, BS♦
Xin Han, MD (Laboratory Medicine)
Cheryl F. Hirsch-Ginsberg, MD (Laboratory Medicine)
Sandra B. Horowitz, PharmD (Pharmacy)
Michael Kroll, MD (Benign Hematology)Ŧ
Amy Pai, PharmD♦
Katy M. Toale, PharmD (Pharmacy)
Mary Lou Warren, DNP, RN, CNS-CC♦
Ali Zalpour, PharmD (Pharmacy)

Ŧ Core Development Team Leads
♦ Clinical Effectiveness Development Team