GUIDELINES FOR ANTITHROMBIN USE AT UCDMC

I. GENERAL GUIDELINES

A. For individual patients in whom anti-thrombin (AT) use is being considered, the physician must contact the Clinical Pharmacology Consult Service (CPCS) for approval before the drug is released from the pharmacy.

B. All patients receiving anti-thrombin will then be monitored by the CPCS service.

II. ANTITHROMBIN DEFICIENCY

A. Acute thrombosis

In any patient with an acute thrombosis in whom a therapeutic APTT cannot be achieved despite large doses of heparin (> 25 units/kg/hour) and in whom the anti-thrombin level is less than 60% of normal, use of a direct IIa inhibitor or a direct Xa inhibitor should be considered as a replacement for heparin.

Anti-thrombin use shall be reserved for use only in patients in whom a continuous infusion of a direct thrombin inhibitor (DTI) is not feasible. Patients in high risk situations may include:

1. Following major surgery, major trauma, underlying inflammatory disease

   Any patient in whom pharmacologic VTE treatment can not be administered using a DTI or direct acting oral anticoagulant.

2. Pregnancy

   Heparin remains the anticoagulant drug of choice in the prenatal period. Antithrombin use will be considered if a patient is refractory to high doses of heparin or cannot be treated using a DTI. After delivery, the majority of patients can be managed with standard heparin or warfarin therapy. Antithrombin use will be considered only if use of heparin or a DTI is contraindicated in the immediate post-delivery phase, or if the patient is refractory to anticoagulation with high doses of heparin.

B. Currently available data does not support the routine use of anti-thrombin in the following patient groups:

   - Post-surgical patients
   - Trauma patients
   - Liver failure patients
   - Nephrotic syndrome patients
   - Drug-induced
   - Disseminated Intravascular Coagulation (DIC) (See appendix A)

Extracorporeal Life Support (ECLS): In pediatric patients placed on ECLS the AT level can decline. Anticoagulation, typically with heparin, is required to prevent thrombotic complications associated with ECLS. The use of intravenously administered AT can be evaluated for use if requested in the setting of ECLS if measured AT levels drop below 75%. CPCS approval is required.

III. NEONATAL PATIENTS
Preterm infants who have: a) severe systemic disease [respiratory distress syndrome (RDS), necrotizing enterocolitis or sepsis] and anti-thrombin levels that are < 40% of the adult normal value and b) who manifest acute thrombosis, may be candidates for use of intravenous anti-thrombin. These patients must be unresponsive to first-line therapies (heparin or AT replacement using plasma, plasma components) before a trial of anti-thrombin will be considered. Appropriate treatment of all precipitating factors (sepsis, RDS, etc.) must be instituted prior to starting the infusion of anti-thrombin. Patients who are unstable and who cannot tolerate the large volume of normal plasma necessary to increase the level of anti-thrombin may also be candidates for anti-thrombin infusion.

III. ANTITHROMBIN: DOSE AND ADMINISTRATION

A. Dosing is based on the pre-therapy plasma antithrombin level, in order to increase plasma antithrombin to the level found in normal human plasma (100%). Dose can be calculated from the following formula:

$$\text{Units required (IU)} = \frac{[\text{Desired} - \text{baseline AT level} \times \text{weight in kg}]}{1.4}$$

* expressed as % normal level based on functional antithrombin assay

B. As a general dosing guide, each unit per kg anti-thrombin administered should correlate with an increase in anti-thrombin levels by 1.4%.

C. Levels are drawn at baseline and 20 minutes post infusion. Subsequent doses can be calculated based on the recovery of the first dose. Plasma antithrombin levels initially should be monitored at least every twelve hours and before the next infusion to maintain plasma antithrombin levels > 70%. In some cases (postoperative, hemorrhage, acute thrombosis), the half-life of the antithrombin may be shortened and require more frequent monitoring.

D. Antithrombin is administered by intravenous infusion over 10-20 minutes. The drug should be administered within three hours of reconstitution.

VI. ANTICOAGULATION THERAPY

In patients with AT deficiency requiring anticoagulation therapy, indirect anticoagulants such as unfractionated heparin, low molecular-weight heparins and fondaparinux may not achieve desired anticoagulation effects. Alternative agents include parenteral direct thrombin inhibitors for short acting therapy, and in more stable patients the direct acting oral anticoagulants (DOAC’s).
Appendix A: Using antithrombin in DIC

1. In the event that antithrombin is requested and approved in the setting of DIC secondary to traumatic shock, the following approach to its use is suggested.

2. Patients with DIC due to traumatic shock must meet the following guidelines before antithrombin use will be considered:

   a. They must be experiencing GROSS bleeding from PREVIOUSLY hemostatic sites including two or more of the following:
      i. IV sites
      ii. Mucous membranes
      iii. Wounds
      iv. Foley catheter
      v. Chest tube
      vi. Endotracheal tube

      **Note: Does not include NG tube bleeding**

   b. The physician must judge that the patient’s underlying injuries are compatible with survival.

   c. Patients will be within seven days of initial trauma.

   d. Patients will have antithrombin levels and DIC panel drawn prior to institution of therapy. When results are available prior to therapy, antithrombin level should be less than 70% and at minimum, the asterisk (*) items of the DIC laboratory parameters should be considered abnormal.

   DIC Laboratory Parameters
   - PT
   - INR
   - APTT
   - Platelets*
   - Fibrinogen
   - D-Dimer*
   - Fibrin monomer
   - FDP*
   - Antithrombin

3. In addition, if a patient is started on antithrombin, the following guidelines will apply as well:

   a. Patients should have coagulation profiles tested every eight hours, including antithrombin levels and DIC panel.

   b. If the antithrombin level is $\geq 60\%$ or the DIC laboratory parameters are within the normal range, the antithrombin will be discontinued.

   c. Patient will receive 48 hours of therapy with antithrombin.

Approved by UCDHS Pharmacy and Therapeutics Committee 5/2017.