| Category of Antithrombotic | Name          | 1<sup>st</sup> step | 2<sup>nd</sup> step | 3<sup>rd</sup> step | 4<sup>th</sup> step | 5<sup>th</sup> step                  |
|---------------------------|---------------|----------------------|--------------------|--------------------|----------------------|--------------------------------------|
| Vitamin K antagonists     | Warfarin      | Vitamin K 10 mg IV, should be used with other agents as it can take up to a day to normalize INR | PCC 25 IU / Kg IV for INR 1.5-3.9 35 IU/Kg IV for INR 4-6 50 IU/Kg IV for INR >6 Although more expensive than FFP, it proved to be better than FFP | FFP 5-30 mL/Kg | Recheck PT/INR at 1.6 & 24 h If INR >1.5 at 1 h, 2-4 units FFP If INR >1.5 at 6 h, Vitamin K 10 mg IV |
| Direct factor Xa inhibitors | Rivaroxaban   | If ingested within 2 h, give one dose activated charcoal orally | Andexanet Alfa 400mg IV bolus; 480mg IV infusion if last dose >7h 800mg IV bolus; 960mg IV infusion if last dose <7h | PCC  • If Andexanet alpha is not available  • Preferably 4F-PCC (Kcentra) with a dose of 50 units/Kg  • Specific anti-Xa assays are the preferred tests to evaluate the anticoagulant effects of FXa-Is Secondary end point analysis should show normalization of PT and INR | Rivaroxaban and Apixaban are not removed by dialysis |
|                           |               |                      |                    |                    |                     | Aripazine (PER977) It was designed to bind to Heparin & LMWH & FXa-Is & direct thrombin inhibitors. |
|                           | Apixaban      |                      |                    |                    |                     |                                      |
|                           | Edoxaban      |                      |                    |                    |                     |                                      |
| Direct thrombin inhibitors | Dabigatran    | If ingested within 2 h, give one dose activated charcoal orally | Idarucizumab A dose of 5 g divided into 2 doses 2.5 g given IV ≤ 15 minutes apart Approved for the reversal of dabigatran | aPCC (50 units/kg) or 4-factor PCC (50 units/kg) if idarucizumab is not available | Consider emergent dialysis in patient with renal failure |
| Unfractionated Heparin | Heparin | Discontinue heparin infusion if intracranial hemorrhage is suspected or present. | Reverse anticoagulation medications. | Protamine sulfate 1mg for every 100 units of heparin given in the previous 2-3 hours with a maximum single dose of 50mg. If the aPTT remains elevated, repeat the protamine sulfate with a dose of 0.5mg/100 units of UFH. |
|------------------------|---------|--------------------------------------------------------------------------------|--------------------------------------|---------------------------------------------------------------------|
| LMWHs and Heparinoids  | Enoxaprin | Discontinue LMWH infusion if intracranial hemorrhage is suspected or present. | Protamine sulfate 1 mg/100 anti-Xa units of LMWH administered in the past 3–5 half-lives of the drug, up to a maximum single dose of 50 mg. If enoxaparin was given within 8 h, administer protamine sulfate at a dose of 1mg/1 mg of enoxaparin administered (up to a maximum single dose of 50 mg). If enoxaparin was given within 8–12 h, administer it at a dose of 0.5/1 mg of enoxaparin. After 3–5 half-lives have elapsed, protamine is probably not needed. |
| Dalteprain             | Nadroparin | Discontinue LMWH infusion if intracranial hemorrhage is suspected or present. | Protamine sulfate rFVIIa 90 mcg/kg IV once. |
| Tinzaparin             | Danaproid | Discontinue LMWH infusion if intracranial hemorrhage is suspected or present. | Protamine sulfate rFVIIa (90 mcg/kg IV) if protamine is contraindicated |
| Pentasaccharides      | Fondaparinux | Discontinue pentasaccharide infusion if intracranial hemorrhage is suspected or present. | aPCC (20 IU/kg) if aPCC is contraindicated or not available |
| Antiplatelets          | Aspirin | Discontinue antiplatelets if intracranial hemorrhage is suspected or present. | Test platelet functions before doing unnecessary. If testing is not available, empiric platelet transfusion |
|                        | Ibuprofen | A single dose of desmopressin DDAVP 0.4 mcg/kg IV in hemorrhage associated with aspirin/COX-1 inhibitors or ADP |
Dipyridamole
Clopidogrel
Prasugrel
Ticagrelor
Ticlopidine
Cilostazol
Anagrelide
Abiciximab
Eptifibatide
Tirofiban
Vorpaxar

hemorrhage is suspected or present.
platelet transfusion
might be considered, if urgent neurosurgical intervention is due.
receptor inhibitors.

4F PCC - 4 factor prothrombin complex concentrates, ADP - Adenosine diphosphate, aPCC - activated prothrombin complex concentrates, DDAVP - desmopressin, FFP - Fresh frozen plasma, INR - International normalized ratio, IU - International Unit, LWMH - low molecular weight heparin, PCC - prothrombin complex concentrates, rFVIIa - Recombinant factor VIIa, UFH - Unfractionated heparin