Disclaimer for Comprehensive Stroke Center (CSC) Clinical Guidelines

These Guidelines are intended only for informational and/or educational purposes on the latest clinical best practice. They ARE NOT to be considered or utilized as a policy, procedure, protocol, or medical order, and are not intended to replace clinical judgment or determine the care of an individual patient. THE IMPLEMENTATION OF ANY OF THE CLINICAL MEASURES DISCUSSED IN THESE GUIDELINES REQUIRES A SPECIFIC MEDICAL ORDER DOCUMENTED IN THE PATIENT’S MEDICAL RECORD. These Guidelines were prepared and approved by the inter-disciplinary teams from the University of Texas-Health Science Center Department of Neurology, Mischer Neuroscience Institute, and Memorial Hermann Hospital-Texas Medical Center-Comprehensive Stroke Center.

Coagulopathy Reversal Protocol

Please note Kcentra® orders will not be delayed. However, all orders are reviewed by a clinical pharmacist specialist for appropriateness prior to preparation. You may receive a call regarding its use if there are concerns.

- This protocol is not intended for patients receiving Argatroban, Bivalirudin, Enoxaparin, Fondaparinux, or Unfractionated heparin.

Labs for All Coagulopathic Patients

- Order CBC with differential and platelets.
- Order DIC panel.
  - DIC panel consists of PT/PTT/D dimer/Thrombin time/Fibrinogen.
- Consider TEG

Coagulopathy in Patients Actively Bleeding or Requires Emergent Reversal for a Procedure on Warfarin

- Step 1: Administer vitamin K 10 mg IV/NS 50 ml over 30 minutes STAT.
  - Onset of action = 4 – 8 hours and peak effect = 12 – 14 hours.
  - Administer regardless of what was reported to be given at outside facility.
  - Vitamin K will assist in sustaining the effects of Kcentra®
- Step 2: Kcentra®
  - Must be ordered by an attending or fellow (with attending approval)
  - Dosing (Use maximum weight of 100 kg if patient > 100 kg)
    - If INR 1.4 – 3.99 = Give 25 units per kg.
    - If INR 4 – 5.99 = Give 35 units per kg.

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- If INR ≥ 6 Give 50 units/kg.
  - Pharmacy will round downward to the nearest vial.
  - Use is restricted to a single dose. Repeat doses do not improve efficacy and increases risk for thromboembolic complications. Hematology consult required if more than 1 dose is needed.
  - Obtain PT/INR/PTT prior to initiating Kcentra® and 2 hours after administration.

### Notes regarding Kcentra® dosing administration
- Each 500 unit vial contains 400–620 units factor IX. Pharmacy will enter the exact dose provide in factor IX units for billing purposes.
- Kcentra® should be infused through a separate infusion line.
- It is administered by IV infusion at a maximum 210 units/minute.

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**Coagulopathy in Patients Actively Bleeding or Requiring Emergent Reversal for a Procedure on New Oral Anticoagulants**

For off-label use in immediate reversal of Rivaroxaban (Xarelto®), Apixaban (Eliquis®) and Dabigatran (Pradaxa®)

- Dabigatran patients: additional removal with hemodialysis may be warranted. Approximately 50% of Dabigatran may be removed at about 2 hour mark.
- Check a TEG (not rapid TEG). If r-time normal Kcentra® is not required.
- First line: Kcentra®
  - Must be ordered by an attending.
  - Dose = 35 units per kg and is restricted to a single dose. (Use maximum weight of 100 kg if patient > 100 kg)
    - Maximum cumulative dose = 50 units/kg per day.
  - Use is restricted to a single dose. Repeat doses do not improve efficacy and increases risk for thromboembolic complications. Hematology consult required if more than 1 dose is needed.
  - Vial sizes may vary. Pharmacy will round downward to the nearest vial size.
  - Obtain PT/INR/PTT/TEG prior to initiating Kcentra® and 2 hours after administration.

**Coagulopathy in Patients NOT on Warfarin or New Oral Anticoagulants AND Patient is Actively Bleeding**

- Maintain fibrinogen > 200 mg/dL in patients actively bleeding.
  - Replace fibrinogen < 200 mg/dL with cryoprecipitate 10 units. If fibrinogen < 100 mg/dl administer 20 units of Cryo.
  - Check fibrinogen level 2 hours after cryoprecipitate. If fibrinogen < 200 mg/dL administer cryoprecipitate 10 units.

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- If PT or PTT is prolonged and fibrinogen > 200 mg/dL, administer FFP 10 ml/kg; do not administer cryoprecipitate.
- Maintain platelets > 75,000/mm³.
- Check CBC and DIC panel every 8 hours X 24 hours, then daily.
- If above measures have been completed and patient is actively bleeding consider rFVIIa 20 micrograms/kg (10 – 40 micrograms/kg) IV push over 2 minutes X 1.
  - For rFVIIa to be most efficacious ensure pH ~ 7.4 and body temperature > 36°C.
- Check CBC and DIC panel 1 hour after rFVIIa.
- Calculate DIC score daily.

**Emergent Placement of Ventriculostomy NOT on Warfarin or New Oral Anticoagulant**
- INR < 1.5 no therapy
- INR > 1.5 – 1.79 administer FFP 2 units + vitamin K 10 mg IV/NS 50 ml over 30 minutes STAT
- INR ≥ 1.8 – 2.9 administer rFVIIa 1 mg IV push over 2 minutes X 1 (≤ 50 kg; administer 0.5 mg).
- INR ≥ 3 – 5.9 administer rFVIIa 2 mg IV push over 2 minutes X 1 + FFP ~ 10 ml/kg
- INR >6 administer rFVIIa 2 mg IV push over 2 minutes X 1 + FFP ~ 20 ml/kg

**Emergent Placement of Ventriculostomy ON Warfarin or New Oral Anticoagulant**

**Warfarin**
- INR ≤ 1.5 administer vitamin K 10 mg IV/NS 50 ml over 30 minutes STAT
- INR > 1.5 – 1.99 administer FFP 2 units + vitamin K 10 mg IV/NS 50 ml over 30 minutes STAT
- INR ≥ 2 administer Kcentra® per “Coagulopathy in Patients Actively Bleeding or Requires Emergent Reversal for a Procedure on Warfarin” + vitamin K 10 mg IV/NS 50 ml over 30 minutes STAT

**New Oral Anticoagulant**
- Administer Kcentra® per “Coagulopathy in Patients Actively Bleeding or Requires Emergent Reversal for a Procedure on New Oral Anticoagulant”

**Patients on Aspirin and/or Antiplatelets**
- Aspirin
  - Consider one unit single donor platelets
- Plavix (with or without Aspirin)
  - Consider 2 units single donor platelets
- Maintain platelet count > 75,000/mm³.

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Reversal of Alteplase (tPA)

- Stop tPA.
- Check fibrinogen level immediately and every 6 hours X 24 hrs.
- Goal = fibrinogen > 100 mg/dl
- Type and cross
- Administer cryoprecipitate 10 – 20 units before fibrinogen level returns
  - 1 unit increases fibrinogen by 5 -10 mg/dl
  - Repeat cryoprecipitate if needed
  - May use fresh frozen plasma (FFP) in case of no cryoprecipitate (1 unit of cryoprecipitate is made from 1 bag of FFP)
- Administer platelets if platelet < 100,000/mm³
- Activated factor 7 is untested in this situation, and should not be used
- Neurosurgery should be called; however, surgery cannot be done until coagulopathy is corrected and is usually not indicated
- MHH Blood Bank: 713-704-3640

Approval of Factor VIIa or Kcentra® Orders

- Kcentra® or rVIIa must be approved by Neuro ICU attending if patient is in the ICU. Place name/cell number in order comments. Must be ordered by Neurosurgery/Stroke Attending if the patient is in the ED or OR.
- The first dose of Kcentra® or rVIIa does not have to be approved by Dr. Miguel Escobar or a clinical pharmacist specialist if the protocol is being followed. All subsequent doses require approval.
Preparation of all Kcentra® or rVIIa orders will require approval by Teresa Allison, Pharm.D., Sophie Samuel, Pharm.D., or Kenneth Chong, Pharm.D.

**Use with Caution**
- In past 6 months: Ischemic stroke (clinical or imaging evidence), myocardial infarction (clinical or EKG evidence), or venous thromboembolism.
- Patients 65 years or older.

**Contraindications to Use of Recombinant Factor VIIa or Kcentra®**
Consult Dr. Miguel Escobar, Teresa Allison, or Kenneth Chong for approval of rFVIIa or Kcentra® if the patient has one of the following contraindications.

- Patient with secondary ICH related to hemorrhagic infarct or cerebrovenous thrombosis.
- Suspected DIC (per labs) if the patient is coagulopathic or end stage liver disease.
- Kcentra® contains heparin. Do not use in patients with active HIT
- Acute myocardial infarction (MI), acute septicemia, acute crush injury, acute peripheral arterial occlusion, acute thrombotic stroke, acute DVT/PE (within 3 months), or high risk thrombophilia.
  - Lupus anticoagulant/anticardiolipin antibodies.
  - Protein C, Protein S, or Antithrombin deficiency.
  - Homozygous factor V Leiden.
  - Double Heterozygous (Factor V Leiden/ Factor II G20210A Prothrombin mutation).
- Pregnancy.
- In past 30 days: history of TIA, angina pectoris, or limb claudication.
- Known or suspected allergy to the drug.

**Contact Information**

- Miguel Escobar, MD: 281-622-9887; pager 713-764-0073
- Teresa Allison, Pharm.D.: 713-502-4020 or pager 24293
- Sophie Samuel, Pharm.D.: 954-593-7870
- Kenneth Chong, Pharm.D.: 281-910-8006

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