LOS ANGELES COUNTY DEPARTMENT OF HEALTH SERVICES
HARBOR-UCLA MEDICAL CENTER

SUBJECT: CLOTTING FACTOR CONCENTRATES **POLICY NO.** 325E

CATEGORY: Provision of Care	**EFFECTIVE DATE:** 9/14
POLICY CONTACT: Jennie Ung, PharmD	**UPDATE/REVISION DATE:** 11/21
REVIEWED BY COMMITTEE(S): Pharmacy and Therapeutics Committee	

PURPOSE:
To provide guidelines for safe prescribing, storing, and dispensing of clotting factor concentrates, including factor VII, factor VIII, factor IX, antihemophilic factor/von Willebrand factor complex, and 4-factor PCC.

POLICY:
All prescribers are required to follow the clotting factor concentrates prescribing guidelines in the interest of patient safety. Unclear and incomplete orders will be clarified before the orders can be accepted.

PRESCRIBING PROCEDURE:

A. Who may prescribe:
- Anesthesiology Attending
- Cardiothoracic (CT) Surgery Attending
- Emergency Department Attending
- Hematology/Oncology Service Attending
- Medicine and Surgical Critical Care Attending
- Obstetrician/Gynecology Attending

B. Providers not listed above must contact the transfusion medicine, hematology, medical or surgical critical care services for approval.

C. Any clotting factor concentrate orders not meeting the indications outlined below must be approved by the Blood Bank resident (310-501-3840) and attending OR hematology attending or fellow (310-501-9865).

D. Order must include:
- Patient's name, medical record number and weight (kg)
- Clotting factor concentrates (product name)
- Dose must be expressed in units/kg/dose or mcg/kg/dose AND total dose (Example: Pt wt 70kg, dose 15mcg/kg = 1050mcg)
- Route and frequency of administration

REVISED: 1/18
REVIEWED: 4/14, 1/18, 11/21

APPROVED BY:

Anish Mahajan, MD
Chief Executive Officer

Anish Mahajan, MD
Chief Medical Officer

Jason Black, MBA, DNP, RN
Chief Nursing Officer

- Indication, treatment plan and anticipated duration of therapy
- Holding parameters (if applicable)
- If written on order form (i.e. downtime) (Attachment I): ordering physician's name, signature, pager number, unique ID number, date and time

E. Provide product name and amount used prior to visit/admission (if applicable)
F. Range orders are not acceptable.
G. For patients weighing under their ideal body weight (IBW), use actual body weight.
H. For patients weighing over their IBW, use IBW.

To calculate adult IBW:
Patients taller than 5 feet:
Males: IBW (kg) = 50 + (2.3 x height in inches over 5 feet)
Females: IBW (kg) = 45.5 + (2.3 x height in inches over 5 feet)

Patients shorter than 5 feet:
Males IBW (kg) = 50 - (2.3 x height in inches under 5 feet)
Females IBW (kg) = 45.5 - (2.3 x height in inches under 5 feet)

To calculate IBW for patient ages 1 to 18 years,
Patients 5 feet and taller:
For boys: IBW (kg) = 39+ (2.27x height in inches over 5 feet)
For girls: IBW (kg) = 42.2+ (2.27x height in inches over 5 feet)

Patients shorter than 5 feet:
IBW (kg) = [(height in centimeter)^2 x 1.65]/1000

I. Dose rounding
   - Pharmacists may round the dosage up or down to the nearest units of product size (example, Pt wt 70kg, dose written 15mcg/kg = 1050mcg → pharmacy may round down to 1000mcg = 1mg)
   - Pharmacist will enter a clarification order specifying the new dose on patient's medical record.
J. Telephone orders
   - Pharmacist may take telephone order to clarify unclear or incomplete orders.

STORING
Hemostatic Agents and Clotting Factor Concentrates will be stored in accordance to manufacturer's recommendation in the pharmacy.

DISPENSING
Pharmacists will prepare and dispense Hemostatic Agents and Clotting Factor Concentrates in accordance to pharmacy policy and procedures.

ADMINISTRATION
Medication will be administered by the primary nurse; documentation of administration, lot#, expiration of blood factors will be on the medication administration record (MAR).

APPROVED INDICATIONS and dosing guidelines

1. **Recombinant activated Factor VII (rFVIIa)**
   a. Prior authorization form for factor VII (Attachment II) must be completed.
   b. Indication:
      i. Prevention and treatment of bleeding and perioperative management for:
         1. Patients with factor VII deficiency
         2. Patients with factor VIII or IX deficiency and inhibitors
      ii. Life-threatening coagulopathic bleeding (including secondary to trauma)
   c. Initial and additional dosages are based on patient weight and indication

Indication	Initial doses	Additional doses
Factor VII deficiency (prevention or surgery)	15-30 mcg/kg IV	15-30 mcg/kg IV q4-6h until hemostasis is achieved.
Factor VIII or IX deficiency with inhibitors (treatment of bleeding episode)	90-120 mcg/kg IV	90-120 mcg/kg IV q2h* until hemostasis is achieved.
Factor VIII or IX deficiency with inhibitors (minor surgery)	90-120 mcg/kg IV prior to surgery and q2h intraoperatively	90-120 mcg/kg IV q2h* for first 48 hrs and then q4-6h until healing has occurred.
Factor VIII or IX deficiency with inhibitors (major surgery)	90-120 mcg/kg IV prior to surgery and q 2 h intraoperatively	90-120 mcg/kg IV q 2h* for first 5 days and then q4h until healing has occurred.
Life-threatening, coagulopathic bleeding (including trauma)	90-120 mcg/kg IV	90-120 mcg/kg IV up to two additional doses until hemostasis is achieved.
Diffuse intraoperative bleeding	90-120 mcg/kg IV	90-120 mcg/kg IV up to two additional doses until hemostasis is achieved.

* Less frequent dosing may be considered based clinical bleeding and hematology approval

2. **Antihemophilic factor (factor VIII), recombinant or monoclonal antibody purified (human)**
   a. Indication:
      i. Prevention and treatment of bleeding for patients with factor VIII deficiency (hemophilia A)
      ii. Perioperative management of patients with factor VIII deficiency
   b. Either recombinant or monoclonal antibody purified may be dispensed depending on the formulation the patient receives at home.
   c. Dosage is based on indication (and desired level increase of factor VIII) and patient weight. Frequency of dosage is based on indication (see table below).
   d. Maintenance doses and further frequency/duration may be adjusted based on individual patient's clinical course and hematologist's recommendations.

Number of AHF units needed = Body weight (kg) x desired Factor VIII increase (% normal) x 0.5

Indication	Desired Factor VIII increase (% normal)	Frequency **
Mild hemorrhage	40-60	20 – 30 units/kg IV q12-24h for 1-3 days
Moderate hemorrhage	40-60	20-30 units/kg IV q8-12h for 3 days then 15 – 25 units/kg for 1-5 days until bleeding resolves

Severe hemorrhage	80-100	40 – 50 units/kg IV q8-12h for 3 days then 15 – 30 units/kg IV for 1-7 days until bleeding resolves
Minor surgery	30-60	15-30 units/kg IV q12h; a single infusion may be adequate
Major surgery	80-100 one hour prior to surgery	Start 40 – 50 units/kg IV q8-12h for 3 days. Maintain factor VIII levels at >30% for 10-14 days post-operatively

** May adjust doses using measured factor levels as needed.

3. **Factor IX, recombinant or monoclonal antibody purified (human)**
   a. Indication:
      i. Prevention and treatment of bleeding in patients with factor IX deficiency (hemophilia B or "Christmas Disease").
      ii. Perioperative management of patients with factor IX deficiency.
   b. Either recombinant or monoclonal antibody purified may be dispensed depending on the formulation the patient receives at home.
   c. Dosage is based on indication (and desired level increase of factor IX) and patient weight. Frequency of dosage is based on indication (see table below).

Number of Factor IX units needed = Body weight (kg) x desired Factor IX increase (% normal) x1.2-1.4 (individual patients on some products may need 20-40% more factor IX, depending from recovery, i.e. pharmacokinetic variability and clinical course)

Indication	Desired Factor VIII increase (% normal)	Frequency **
Minor to moderate hemorrhage	20-50	Repeat dosage twice daily until bleeding stops
Severe hemorrhage	50-100	Repeat dosage twice daily for 3-5 days, up to 10 days
Surgery	50-100	Repeat dosage twice daily for 7-10 days or until healing has been achieved.

** May adjust doses using measured factor levels as needed.

4. **Antihemophilic factor/von Willebrand factor complex (human)**
   a. Indication:
      i. Prevention and treatment of bleeding in patients with factor VIII deficiency (hemophilia A)
      ii. Treatment of bleeding episodes and perioperative management of patients with:
         1. Mild to moderate von Willebrand disease where use of desmopressin (DDAVP) is known or suspected to be inadequate or contraindicated.
         2. Severe von Willebrand disease
   b. Dosage is based on indication (and desired level increase of factor VIII or von Willebrand factor), patient weight and ratio of vWF:FactorVIII in the formulation. Frequency of dosage is based on indication (see table below).

Indication	Dosage	Frequency **
Minor hemorrhage	15-25 units Factor VIII/kg IV	May only require one dose; may repeat half the initial dose once or twice daily for 1-2 days
Moderate hemorrhage or minor surgery	20 - 30 units Factor VIII/kg IV	20 - 30 units Factor VIII/kg IV q8-12h for 1-2 days, then twice daily for 7-10 days or until healed
Severe hemorrhage or major surgery	40-50 units Factor VIII/kg IV	40-50 units Factor VIII/kg IV q8-q12h for 3 days, then twice daily for 7-10 days or until healed

** May adjust doses using measured factor levels as needed.

5. **4-factor PCC (Prothrombin Complex Concentrate, Human)**
   a. Prior authorization form for 4-factor PCC (Attachment III) must be completed.
   b. Indication:
      i. Intracranial hemorrhage or
      ii. Bleeding from any anatomic site that is thought to be immediately life threatening or
      iii. Urgent surgery/invasive procedure with high INR
      AND
      iv. History of recent exposure to warfarin or factor Xa inhibitors (i.e., rivaroxaban, apixaban, edoxaban, fondaparinux)
      OR
      v. Excessive bleeding post cardiopulmonary bypass which is uncontrolled by conventional measures and patient received minimum of 2 units of fresh frozen plasma and 1 unit of platelets
   c. Dosage is based on patient weight
   d. Contraindicated/not recommended for (including, but not limited to):
      - Patients with Heparin Induced Thrombocytopenia (HIT).
      - Patients with Disseminated Intravascular Coagulation (DIC).
      - Anaphylactic or severe systemic reaction to product or any of its components, including heparin, factors II, VII, IX, or X, proteins C or S, antithrombin 3, or human albumin
      - For reversal of direct thrombin inhibitors (e.g. dabigatran)
   e. In an emergency situation, pharmacist may dispense product prior to authorization form being filled, if it meets the inclusion criteria and no exclusion criteria.
   f. 4-factor PCC will be given in combination with supportive care (i.e. for warfarin-associated bleeding, use IV vitamin K; for factor Xa inhibitors-associated bleeding, use tranexamic acid or aminocaproic acid; oral activated charcoal is an option, if last factor Xa inhibitor dose was within 2 hours of ingestion).
   g. Only a single dose of 4-factor PCC will be used.

4-factor PCC (Prothrombin Complex, Human)—prior authorization required	
Pre-treatment INR	**Dosing for patients on warfarin therapy**
INR 2 to 4	25 units Factor IX x _____kg = _____units IV x1 (Max 2500 units factor IX)
INR 4 to 6	35 units Factor IX x _____kg = _____units IV x1 (Max 3500 units factor IX)
INR greater than 6	50 units Factor IX x _____kg = _____units IV x1 (Max 5000 units factor IX)

4-factor PCC (Prothrombin Complex, Human) – prior authorization required	
Dosing for patients on Factor Xa inhibitors (i.e., rivaroxaban, apixaban, edoxaban, fondaparinux) *limited data for optimal dose in this setting	25 units/kg (2500 units max) Or 50 units/kg (5000 units max)
Dosing for excessive bleeding in cardiopulmonary bypass *limited data for optimal dose in this setting	25 units/kg (2500 units max)

Revised and Approved by:
Medical Executive Committee on 11/2021

Beverley A. Petrie

Beverley A. Petrie, M.D.
President, Professional Staff Association

COUNTY OF LOS ANGELES

DEPARTMENT OF HEALTH

HARBOR-UCLA MEDICAL CENTER
SUPPLEMENTAL PRESCRIBER'S ORDERS

DO NOT USE FOR ADMISSION OR TRANSFER ORDERS

Allergy Status:	Weight ___/___ Height ___/___ Date Obtained:

1		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	
2		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	
3		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	

I.V. FLUID ORDERS, DRIPS, AND ALL OTHER NON-MEDICATION ORDERS:

PROVIDER LAST NAME:	PROVIDER SIGNATURE:	NOTED BY:	DATE/TIME:
DATE: / TIME: AM PM	PROVIDER I.D. NUMBER: / PAGER NUMBER:	TRANSCRIBED BY (IF OTHER THAN R.N.):	DATE/TIME:

1		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	
2		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	
3		(DOSE)	(UNIT)	(ROUTE)
	☐ Discontinue ☐ PRN & indication:	(FREQUENCY)	DOSE BY WEIGHT (OR "N/A")	

I.V. FLUID ORDERS, DRIPS, AND ALL OTHER NON-MEDICATION ORDERS:

PROVIDER LAST NAME:	PROVIDER SIGNATURE:		
DATE: / TIME: AM PM	PROVIDER I.D. NUMBER:	PAGER NUMBER:	
NOTED BY:	DATE:	TIME:	
TRANSCRIBED BY (IF OTHER THAN R.N.):	DATE:	TIME:	

Attachment II

Health Services
LOS ANGELES COUNTY

Off-Label Recombinant Factor VIIa (NovoSeven®) Authorization Form

Instructions:

1. Please complete all sections of this form. Incomplete forms will be returned to the prescriber.
2. This form is not a substitute for a blood bank order. Any form submitted without a blood order will be considered incomplete.
3. Submit this form accompanying the blood bank order.
4. If criteria are not met, the blood bank will not dispense recombinant factor VIIa.
5. Recombinant Factor VIIa is intended for salvageable patients with on-going life-threatening bleeds.
6. All recombinant Factor VIIa requests will be evaluated on a case by case basis.

EXCLUSION CRITERIA (If any of the following criteria apply, the patient does NOT qualify for recombinant Factor VIIa use)		
1) Unsalvageable patients 2) For the reversal of the new oral anti-coagulants: Dabigatran, Rivaroxaban, and Apixaban)		
FIRST DOSE APPROVAL CRITERIA (Check ALL criteria that apply, ALL lines must be checked for approval. None of the exclusion criteria above apply.) **Note: Any incomplete information MAY AFFECT THE OUTCOME of this request.**		
☐	Patient meets massive transfusion criteria : OR **> 6 Units of PRBC within 1 hour** **> 10 Units of PRBC within 24 hours**	
☐	Surgical bleeding has been controlled	
☐	Patient's body temperature is > 36.5°C	
☐	Patient's platelet is > 50K	
☐	Patient's pH is > 7.20	
☐	Patient is coagulopathic: OR **INR > 2** **Suspected / Documented Coagulopathy**	
☐ Trauma Surgery	☐ Cardiac Surgery	☐ Spinal Procedure
SECOND DOSE APPROVAL CRITERIA (Check ALL criteria that apply, ALL lines must be checked for approval. None of the exclusion criteria above apply.)		
☐	Patient responded to first dose of Recombinant Factor VIIa	
☐	Patient last received Recombinant Factor VIIa at least 2 hours ago	

PRESCRIBER INFORMATION		
Attending Name (Printed)		Attending Signature
Attending ID#	Specialty/Services	
Telephone/Pager#	Date and Time	*I declare that the information this form, to my best knowledge and belief, is true, correct, and complete*

ATTACH TO BLOOD BANK ORDER	
Blood Bank Review: Approval criteria met? ☐ YES ☐ NO	
Date and Time Received	Date and Time Dispensed
Blood Bank Reviewer:	

Health Services

4-factor Prothrombin Complex Concentrate (Kcentra®) Prior Authorization Form

Instructions

1. Please complete all sections of the form. Incomplete forms will be returned to the prescriber.
2. Submit form along with the prescription order to the facility pharmacy. This form is not a substitute for a prescription order. Any form submitted without an order will be considered incomplete and not reviewed.
3. Inpatient/Clinic use. CMO or designee approval is not needed for cases where the criteria are met. If all criteria below are not met, form will be forwarded by the facility pharmacy to DHS Pharmacy Affairs for review. The CMO or designee will provide final decision in these cases.

Notes

1. This prior authorization form must be submitted with **ALL** written inpatient prescriptions.
2. Please complete ALL areas below, as incomplete prior authorization requests MAY AFFECT THE OUTCOME of this request.
3. Prothrombin Complex Concentrate is not intended for reversal of the direct thrombin inhibitors.

STEP 1: EXCLUSION CRITERIA *(If any of the following criteria apply, the patient does NOT qualify for Prothrombin Complex Concentrate use. Please check off each box on the left to indicate that patient doesn't meet exclusion criteria)*	
☐	Known anaphylactic or severe systemic reactions to Kcentra® or any components in Kcentra® including heparin, Factors II, VII, IX, X, Proteins C and S, Antithrombin III and Human albumin
☐	Patients with disseminated intravascular coagulation (DIC)
☐	Patients with known heparin-induced thrombocytopenia (HIT)
☐	For the reversal of dabigatran
STEP 2: APPROVAL CRITERIA *(Check ALL criteria that apply). ALL lines must be checked for approval. None of the exclusion criteria above apply.)* **Note: Any incomplete information MAY AFFECT THE OUTCOME of this request.**	
☐	Patient is currently on warfarin therapy OR factor Xa inhibitors therapy (i.e., rivaroxaban, apixaban, or edoxaban)
☐	Patient requires urgent reversal of VKA anticoagulation OR factor Xa inhibitors and • has acute active, life-threatening bleeding (e.g. intracranial hemorrhage) OR • requires emergency surgical intervention (and supratherapeutic INR in warfarin patients)
☐	Kcentra® will be given in combination with supportive care (i.e. for warfarin associated bleed use IV vitamin K, for factor Xa bleed use tranexamic acid or aminocaproic acid, oral activated charcoal an option if last factor Xa inhibitor dose within 2 hours of ingestion)
☐	Only a single dose of Kcentra® will be used
OR	
☐	For use in excessive bleeding post cardiopulmonary bypass which is uncontrolled by conventional measures AND
☐	Patient has received at minimum 2 units of fresh frozen plasma and 1 unit of platelets AND
☐	Attending is a cardiac surgeon or a cardiac anesthesiologist AND
☐	Only a single dose of Kcentra® will be used

STEP 3: DOSAGE *(Check the appropriate dosage)*

Dosing for Patients on Warfarin Therapy	Dosing for Patients on Factor Xa Inhibitors (i.e., rivaroxaban, apixaban, edoxaban) *limited data for optimal dose in this setting	Dosing for Excessive Bleeding in Cardiopulmonary Bypass *limited data for optimal dose in this setting
☐ 25 units/kg (2500 units max, recommended in INR 2 to less than 4) ☐ 35 units/kg (3500 units max; recommended in INR 4 to 6) ☐ 50 units/kg (5000 units max; recommended in INR greater than 6)	☐ 25 units/kg (2500 units max) ☐ 50 units/kg (5000 units max)	☐ 25 units/kg (2500 units max)

STEP 4: ADDITIONAL EXPLANATION *(For additional comments, please attach to form)*

STEP 5: PRESCRIBER INFORMATION

Prescriber Name (Printed):		Prescriber Signature Date _____ *I declare that the information on this form, to my best knowledge and belief, is true, correct, and complete.*
Prescriber NPI #:	Clinic/Ward:	
Direct Telephone/Pager #:	Email:	

STEP 6: ATTACH TO PRESCRIPTION ORDER

Pharmacy Review: Approval criteria met? ☐ YES ☐ NO See instructions at top of form for next step following review	
Date Received:	Date of Decision:
Pharmacist Reviewer:	
Medical Review: ☐ Approved ☐ Denied	
Date Received:	Date of Decision:
CMO or Designee:	

Product Information: Kcentra® lyophilized powder for reconstitution, prothrombin complex concentrate, CSL Behring, Marburg, Germany