

ANTICOAGULATION USE SAFETY

Patti Romeril, PharmD

Anticoagulant Reversal for Emergent Surgery/Procedure Order Set

Current Houston Methodist practice for anticoagulant reversal agent ordering leaves room for variability with the options to select several standalone orders or multiple order sets. In order to streamline this process and minimize errors, the proposal to create a “reversal of anticoagulation prior to emergent procedure/surgery” order set” has been approved. A summary of the accepted changes are listed below along with visual aids to demonstrate the process of ordering within Epic.

Summary of Accepted Changes:

Reversal of apixaban, rivaroxaban, edoxaban: add “prolonged reversal” and “andexanet alfa prior to procedures when heparin is required” statement

▼ Medications and Additional Laboratory

▼ **Reversal for associated anticoagulant**

apixaban (ELIQUIS), rivaroxaban (XARELTO), edoxaban (SAVAYSA)

- **Prolonged reversal:** Andexanet alfa has NOT been studied for anticoagulant reversal prior to procedure due to its short half-life with anti-FXa activity increasing after the 2-hours infusion. If need for prolonged reversal is anticipated, please consider use of prothrombin complex concentrate (KCentra)
- **Andexanet alfa prior to procedures where heparin is required:** Using andexanet alfa prior to surgery could lead to heparin resistance or unresponsiveness secondary to andexanet alfa binding to heparin-activated anti-thrombin. If heparin will be used during the procedure, please consider use prothrombin complex concentrate (KCentra)

Medications

- Andexanet alfa (Andexxa®) infusion (RESTRICTED) - **when prolonged reversal (>2 hours) NOT REQUIRED and/or heparin WILL NOT be used during procedure**
- STAT Prothrombin complex concentrate (KCentra) IV - **when prolonged reversal (>2 hours) REQUIRED and/or heparin WILL be used during procedure**



Andexanet alfa (Andexxa®) infusion (RESTRICTED)

| Fxa Inhibitor | Fxa Inhibitor Last Dose | Timing of Fxa Inhibitor Last Dose Before Andexanet alfa Initiation | |
|---------------|-------------------------|--|----------|
| | | <8 Hours or Unknown | ≥8 Hours |
| Apixaban | ≤5 mg | Low dose | Low dose |
| | >5 mg or unknown | High dose | |
| Rivaroxaban | ≤10 mg | Low dose | |
| | >10 mg or unknown | High dose | |

High dose should also be used for patients ≤7 hours since last administration of treatment dose enoxaparin ≥ 1 mg/kg in a patient allergic to protamine.

- Low Dose Option
- High Dose Option

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Summary of Accepted Changes (cont.):

Reversal of apixaban, rivaroxaban, edoxaban: Andexanet alfa selection– add sodium chloride 0.9 bolus following administration; add specific order questions

apixaban (ELIQUIS), rivaroxaban (XARELTO), edoxaban (SAVAYSA)

Medications

Andexanet alfa (Andexxa®) infusion (RESTRICTED)

| Fxa Inhibitor | FXa Inhibitor Last Dose | Timing of FXa Inhibitor Last Dose Before Andexanet alfa Initiation | |
|---------------|-------------------------|--|----------|
| | | <8 Hours or Unknown | ≥8 Hours |
| Apixaban | ≤5 mg | Low dose | Low dose |
| | >5 mg or unknown | High dose | |
| Rivaroxaban | ≤10 mg | Low dose | |
| | >10 mg or unknown | High dose | |

High dose should also be used for patients ≤7 hours since last administration of treatment dose enoxaparin ≥ 1 mg/kg in a patient allergic to protamine.

Low Dose Option

Central Line Administration

Peripheral Line Administration

Low Dose Option

Central Line Administration

andexanet alfa (ANDEXXA) Low Dose Central Line IV Bolus (RESTRICTED)

400 mg, intravenous, at 160 mL/hr, Administer over 15 Minutes, once, today at 1430, 1 dose
 Do not exceed 30 mg/min for bolus rate.

Followed By

andexanet alfa (ANDEXXA) Low Dose 480 mg Central Line infusion (RESTRICTED)

4 mg/min (24 mL/hr), intravenous, Administer over 120 Minutes, once, today at 1445, 1 dose
 Central Line Administration Only
 Infusion will require a 0.2 or 0.22 micron in-line polyethersulfone or equivalent low protein binding filter.

Followed by

sodium chloride 0.9 % bolus 50 mL

50 mL, intravenous, at 600 mL/hr, Administer over 5 Minutes, once, today at 1830, For 1 dose
 Administer 50 mL through the SAME line that the Andexxa infusion was administered through (to flush the line)

Andexanet alfa is restricted to attending-level physicians. Are you an attending-level physician or ordering on behalf of one?

YES, I am an approved provider I am ordering on behalf of an approved provider

Name of Approved Provider:

Andexanet alfa has NOT been studied for anticoagulant reversal prior to procedure due to its short half-life with anti-FXa activity increasing after the 2-hours infusion. Is need for prolonged reversal (>2 hours) anticipated?

HARD STOP Yes - Please consider 4F-PCC (Kcentra®) No - OK to use andexanet alfa

Using andexanet alfa prior to surgery could lead to heparin resistance or unresponsiveness secondary to andexanet alfa binding to heparin-activated anti-thrombin. Will heparin be used during the procedure?

HARD STOP Yes - Please consider 4F-PCC (Kcentra®) No - OK to use andexanet alfa

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Summary of Accepted Changes (cont.):

Reversal of apixaban, rivaroxaban, Edoxaban: Change Prothrombin complex concentrate dosing to 1,000 units and 2,000 units (default dose)

apixaban (ELIQUIS), rivaroxaban (XARELTO), edoxaban (SAVAYSA)

Medications

STAT Prothrombin complex concentrate (KCentra) IV

Avoid use in disseminated intravascular coagulopathy (DIC). May contain heparin, avoid use in heparin induced thrombocytopenia (HIT). Closely monitor for thromboembolic events during and after administration. Use has not been evaluated in patients who have experienced a thromboembolic event, MI, CVA, TIA, unstable angina, or severe peripheral vascular disease within the prior 3 months.

prothrombin complex human (KCENTRA) injection
intravenous, once, today at 1530, 1 dose
For Pharmacy Documentation Only:
Dose rounded to ___ (unit) based on actual stock drug concentration(s) of ___ (unit) or ___ (units/mL).

! A total of ___ vials were used.
Total volume to be infused = ___ mL

Administer at a rate of 504 mL/hr (0.12 mL/kg/min). Do not exceed 504 mL/hr.

Recommended dosing:

- Radio buttons for 1,000 units and 2,000 units – default selection 2,000 units

Removal of idarucizumab for dabigatran reversal standalone orders

! Reversal for associated anticoagulant

dabigatran (PRADAXA)

Consult Nephrology/Hyperten

idaruCIZUmab (PRAXBIND)

Note: For Hereditary Fructose Intolerance Patients - idarucizumab contains 4 gm of sorbitol as an excipient

2.5 gram x 2 doses = 5 grams total dose delivered

idaruCIZUmab (PRAXBIND) IVPB solution 2.5 g
2.5 g, intravenous, at 300 mL/hr, Administer over 10 Minutes, every 10 min, First dose today at 1500, Last dose today at 1510, 2 doses.
Administer 2.5 grams x 2 doses for a total dose of 5 grams delivered. Administer no more than 15 minutes apart.

- Remove dabigatran as a standalone order

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Summary of Accepted Changes (cont.):

Removal of protamine for heparin reversal standalone orders

▼ Medications and Additional Laboratory

▼ **Reversal for associated anticoagulant**

heparin

Medications

MAX single dose of protamine IV should not exceed 50 mg

● Protamine for one-time dose of Heparin (i.e. bolus)

Exposure to heparin **less than 30 minutes ago**, give 1 mg of protamine for every 100 units of unfractionated heparin.
 Exposure to heparin **30-60 minutes ago**, give 0.5 mg of protamine for every 100 units of unfractionated heparin.
 Exposure to heparin was **greater than 2 hours ago**, give 0.25 mg of protamine for each 100 units of unfractionated heparin

Degree of reversal can be expressed with aPTT and/or anti-factor Xa Activity.

Use with caution in patients with a history of vasectomy, previous exposure to protamine through protamine-containing insulins or with known fish allergy.
 Do NOT exceed a dose rate of 5 mg/minute. MAX Dose of protamine is 50 mg.

● Protamine for prolonged exposure of Heparin (i.e. IV infusion)

Use only the last 3 hours of heparin exposure prior to reversal when considering the total amount of heparin administered to the patient

- For every 100 units of heparin patient received in last hour give 1 mg of protamine
- For every 100 units of heparin the patient received in the 2nd hour, give 0.5 mg of protamine
- For every 100 units of heparin the patient received in the 3rd hour, give 0.25 mg of protamine

Degree of reversal can be expressed with aPTT and/or anti-factor Xa Activity. **Contact pharmacy** if assistance is required in determining amount of heparin administered to the patient over time.

Use with caution in patients with a history of vasectomy, previous exposure to protamine through protamine-containing insulins or with known fish allergy.
 Do NOT exceed a dose rate of 5 mg/minute. MAX Dose of protamine is 50 mg.

protamine injection

intravenous, once, today at 1515, 1 dose

- ⚠ Do not exceed a dose administration rate of 5 mg/min.
 ADMINISTER AT A RATE OF 5 MG/MIN

- **Remove protamine as a standalone order**

Reversal of enoxaparin or dalteparin: refer to andexanet alfa changes– same order questions and hard stops for prolonged reversal and heparin during procedure

⚠ **Andexanet alfa** is restricted to attending-level physicians. Are you an attending-level physician or ordering on behalf of one?

YES, I am an approved provider I am ordering on behalf of an approved provider

⚠ Name of Approved Provider:

⚠ **Andexanet alfa** has NOT been studied for anticoagulant reversal prior to procedure due to its short half-life with anti-FXa activity increasing after the 2-hours infusion. Is need for prolonged reversal (>2 hours) anticipated?

HARD STOP Yes - Please consider 4F-PCC (**Kcentra**®) No - OK to use **andexanet alfa**

⚠ Using **andexanet alfa** prior to surgery could lead to heparin resistance or unresponsiveness secondary to **andexanet alfa** binding to heparin-activated anti-thrombin. Will heparin be used during the procedure?

HARD STOP Yes - Please consider 4F-PCC (**Kcentra**®) No - OK to use **andexanet alfa**

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Summary of Accepted Changes (cont.):

Reversal of warfarin: change phytonadione IV dosing to 5mg and 10mg (default dose); Change prothrombin complex human default dosing to 1,000 units and 2,000 units. Use 2,000 units for weight > 100kg, INR > 7.5

Medications and Additional Laboratory

Reversal for associated anticoagulant

fresh Frozen Plasma

- Prepare fresh frozen plasma
Routine
Blood Products, Sign
- Transfuse fresh frozen plasma
Routine
Pre-op, Sign and Hold
- sodium chloride 0.9% infusion
250 mL, intravenous, at 30 mL/hr, continuous, Starting today at 1500, Until Discontinued, Pre-op
Administer with blood
Sign and Hold

phytonadione (vitamin K) (AQUA-Mephyton) IVPB
10 mg, intravenous, once

Recommended vitamin K dosing:
• Radio buttons 5 mg and 10 mg (10 mg pre-selected option)

STAT Prothrombin complex concentrate (KCentra) IV

Avoid use in disseminated intravascular coagulopathy (DIC). May contain heparin, avoid use in heparin induced thrombocytopenia (HIT). Closely monitor for thromboembolic events during and after administration. Use has not been evaluated in patients who have experienced a thromboembolic event, MI, CVA, TIA, unstable angina, or severe peripheral vascular disease within the prior 3 months.

prothrombin complex human (KCENTRA) injection
intravenous, once, today at 1530, 1 dose
For Pharmacy Documentation Only:
Dose rounded to ___ (unit) based on actual stock drug concentration(s) of ___ (unit) or ___ (units/mL).
A total of ___ vials were used.
Total volume to be infused = ___ mL
Administer at a rate of 504 mL/hr (0.12 mL/kg/min). Do not exceed 504 mL/hr.

Recommended Kcentra® dosing:
• Radio buttons 1,000 units and 2,000 units
• Use 2,000 units for weight >100 kg, INR >7.5

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