Anticoagulation and Reversal Agents in the Hospitalized Patient

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Disclosures

- No relevant commercial relationships to disclose.

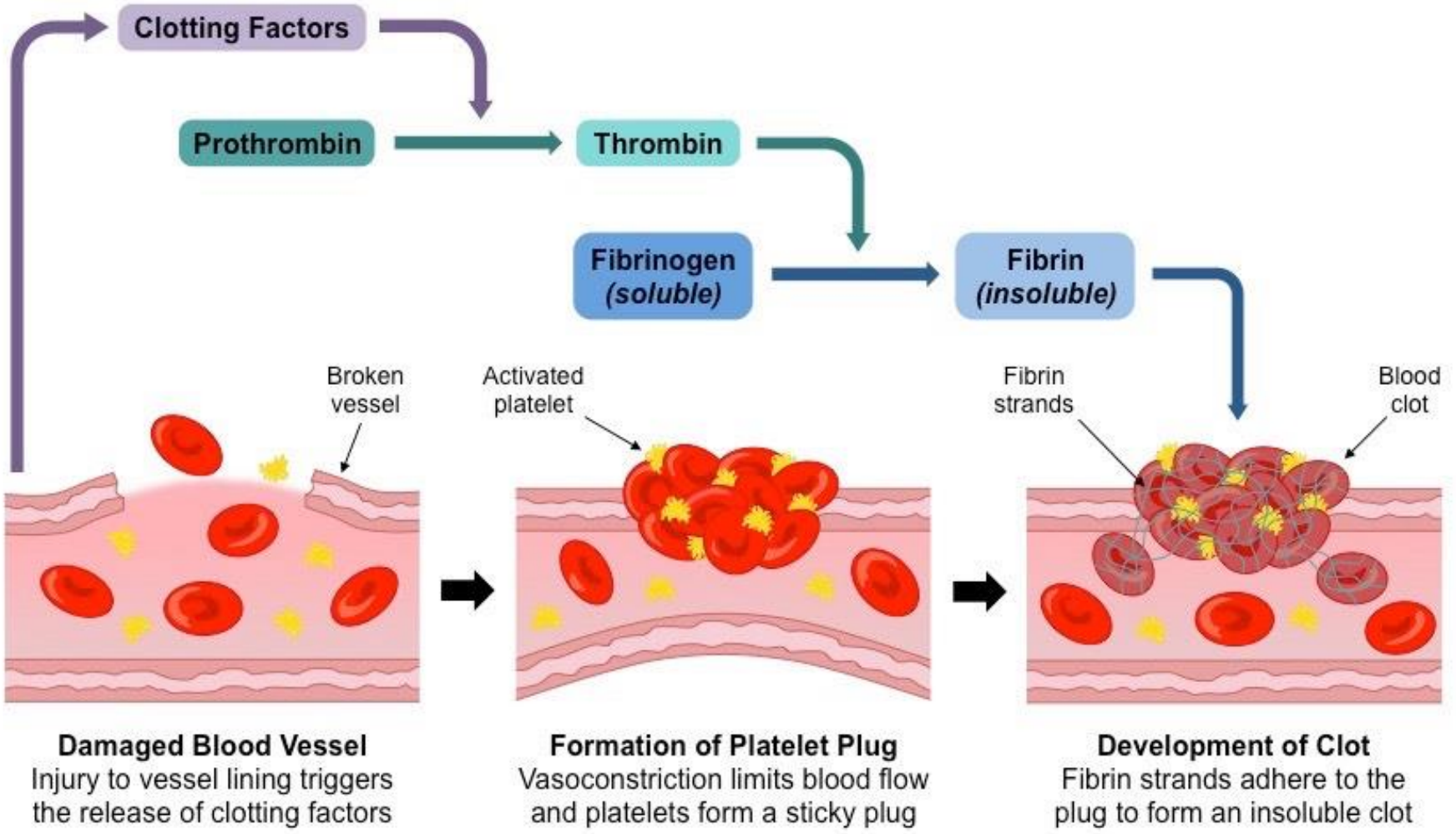
Learning Objectives

At the conclusion of this session, participants should be able to:

1. Identify the mechanism of action of each anticoagulant and where it inhibits the clotting cascade
2. Describe risks, advantages, and disadvantages of each reversal agent and blood product
3. Identify the reversal agents approved for each of the anticoagulants
4. Given patient specific factors, recommend the appropriate reversal agent and a comprehensive monitoring plan

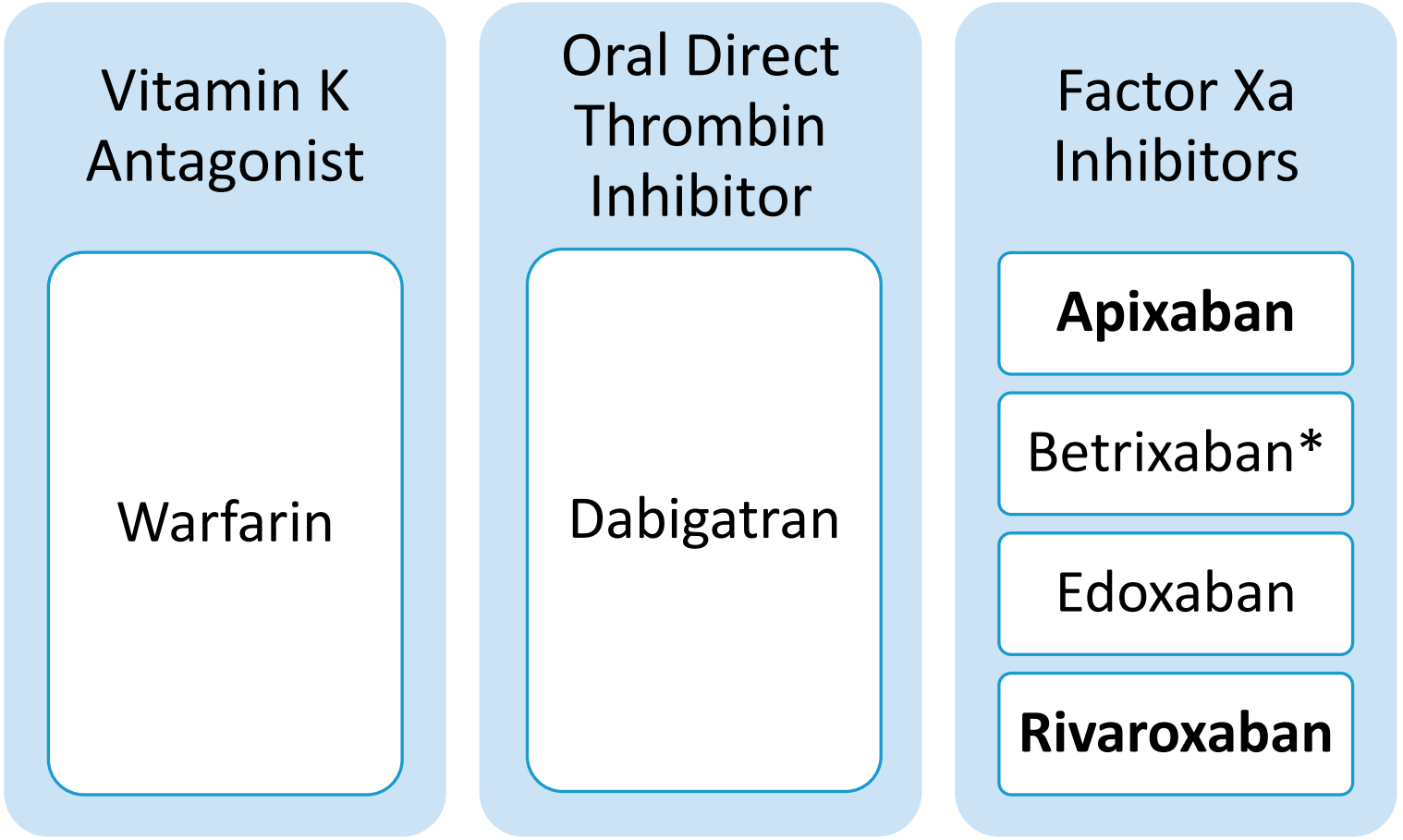
Background

Clotting Cascade



https://ib.bioninja.com.au/standard-level/topic-6-human-physiology/63-defence-against-infectio/clotting.html

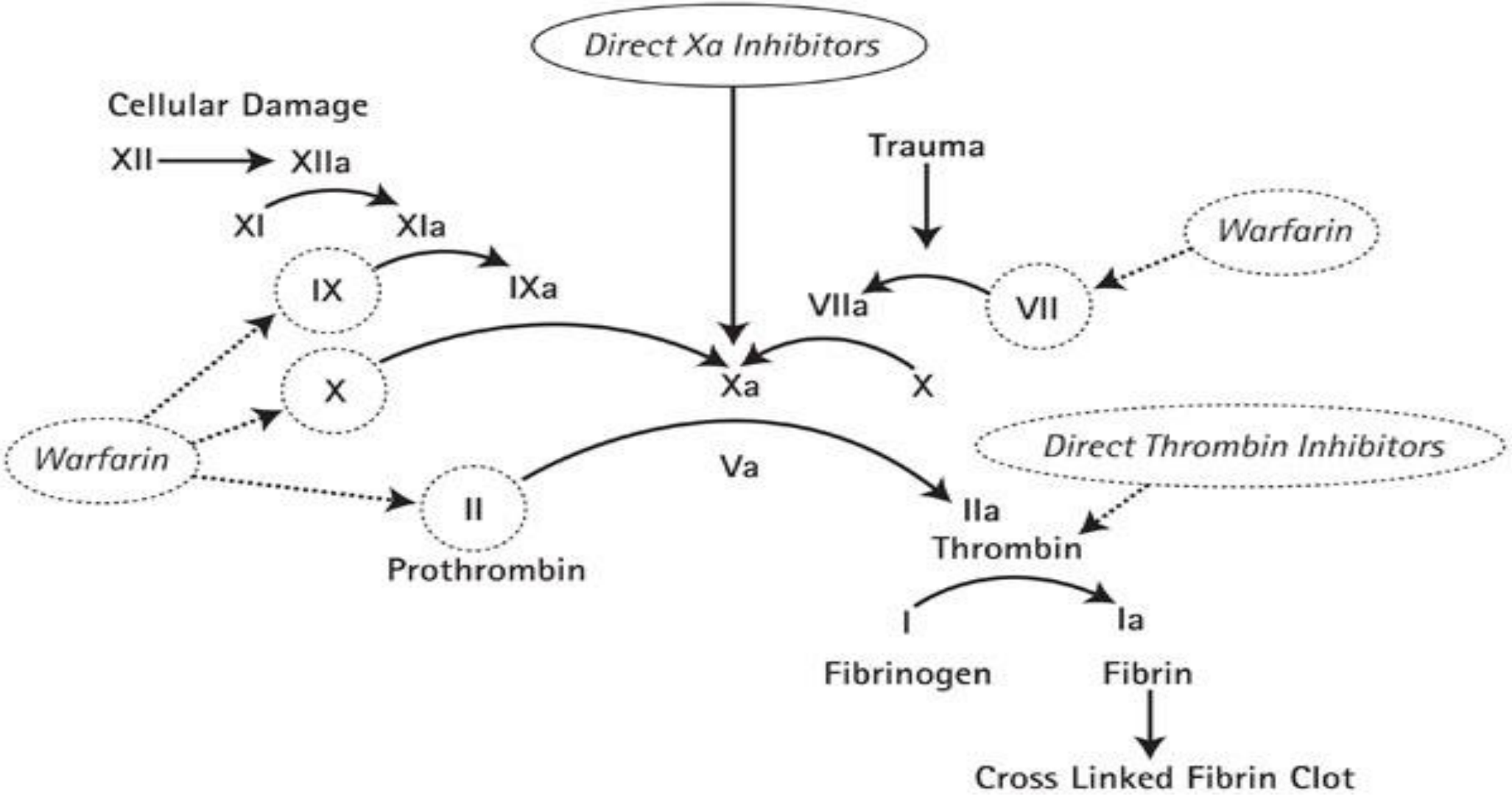
Oral Anticoagulants



*Removed from the market in April 2020

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.

Oral Anticoagulants



http://www.nature.com/bdj/journal/v215/n1/images/sj.bdj.2013.628-f1.jpg

Reversal Agents

Reversal Agent	Brand Name	Anticoagulant
Vitamin K		Warfarin
4-Factor Non-activated Prothrombin Complex Concentrate (PCC)	**Kcentra®**	Warfarin Factor Xa Inhibitors*
Idarucizumab	**Praxbind®**	Dabigatran
Andexanet alfa	**Andexxa®**	Apixaban
		Rivaroxaban

*Not FDA-approved for Factor Xa inhibitor reversal

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.

Factor & Blood Products

Product	Brand Name	Contents
Fresh Frozen Plasma (FFP)		Non-activated factors II, V, VII, VIII, IX, X, XI, XIII, VWF
Non-activated four factor PCC	Kcentra®	Factors II, VII, IX, and X Protein C and S
Activated three factor prothrombin complex concentrate	FEIBA®	Non-activated factors II, IX, and X Activated factor VII
Recombinant factor VII	NovoSeven®	Activated factor VII
Cryoprecipitate		Factors I, VIII, XIII, VWF

Pharmacotherapy: A Pathophysiologic Approach, 9e. New York, NY: McGraw-Hill; 2014.

Factor & Blood Products

Product	Risks and Contraindications
Fresh Frozen Plasma (FFP)	• High volume content • Potential to cause TRALI*, anaphylactic reactions, urticaria
Non-activated four factor PCC	• Black box warning for thromboembolic events • Contraindicated in patients with HIT or DIC
Activated three factor PCC	• Black box warning for arterial and venous thromboembolic events • Contraindicated in patients with HIT or DIC
Recombinant factor VII	• Black box warning for arterial and venous thromboembolic events
Cryoprecipitate	• Potential to cause TRALI*, anaphylactic reactions, urticaria

*TRALI: transfusion related acute lung injury

Vitamin K Antagonist: Warfarin

Warfarin (Coumadin®)

- Inhibits vitamin K epoxide reductase and synthesis of vitamin K dependent clotting factors
  - Factors II, VII, IX, and X

- **Indications**
  - Stroke prophylaxis in valvular and nonvalvular atrial fibrillation (AF)
  - Treatment of venous thromboembolism (VTE)
  - Mechanical aortic or mitral valves

http://packageinserts.bms.com/pi/pi_coumadin.pdf
https://www.google.com/url?sa=i&url=https%3A%2F%2Fuihc.org%2Fhealth-topics%2Ffrequently-asked-questions-about-warfarin&psig=AOvVaw2W6q8BDTDpc2yA-DbbNM4a&ust=1629216179977000&source=images&cd=vfe&ved=0CAgQjRxqFwoTCNCE9a_1tfICFQAAAAAdAAAAABAD

Warfarin (Coumadin®)

Adverse Effects

- Bleeding and bruising
- Skin necrosis

Monitoring

- International normalized ratio (INR)
- Signs and symptoms of bleeding
- Hemoglobin
- Hematocrit
- Platelets
- Liver function tests

Pregnancy Category X

http://packageinserts.bms.com/pi/pi_coumadin.pdf

Warfarin (Coumadin®)

Drug Interactions

- Azole antifungals
- Sulfamethoxazole/trimethoprim
- Fluoroquinolones
- Penicillins
- Cephalosporins
- Carbamazepine
- Amiodarone
- Metronidazole
- Rifampin
- Alcohol

http://packageinserts.bms.com/pi/pi_coumadin.pdf

Warfarin Reversal Options

- **Vitamin K**
  - Oral: used for non-urgent reversal
  - Intravenous (IV): potential to cause anaphylactic reactions
  - Subcutaneous (SUBQ): erratic absorption

- **Fresh frozen plasma**
  - Higher fluid content
  - Can only lower INR to ~1.5
  - Must be thawed prior to administration
  - Potential to cause TRALI, urticaria, or anaphylactic reactions

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

Warfarin Reversal Options

- **Kcentra®: non-activated 4-factor PCC**
  - Lower fluid content
  - More expensive
  - More effective INR correction

Baseline INR	Dosing	Cost per dose ($)*
2-3.9	25 units/kg (maximum 2500 units)	7,850
4-5.9	35 units/kg (maximum 3500 units)	10,990
>6	50 units/kg (maximum 5000 units)	15,700

*Based on average wholesale price

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

Warfarin Reversal

- **INR >4.5 but <10 WITHOUT clinically relevant bleeding**
  - HOLD warfarin

- **INR >10 WITHOUT clinically relevant bleeding**
  - HOLD warfarin
  - Administer oral vitamin K
  - Counsel patient to monitor for black, tarry stool, or blood in urine or stool

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

Warfarin Reversal

- **Life-threatening bleeding OR urgent/emergent surgery**
  - HOLD warfarin
  - Administer Vitamin K 10 mg IV over 30 minutes PLUS
    - Fresh frozen plasma (FFP) OR
    - **Kcentra® (preferred)**
  - Monitor INR, hemoglobin, hematocrit, platelets

https://labeling.cslbehring.com/PRODUCT-DOCUMENT/US/Kcentra/EN/Formulary-Kit.pdf

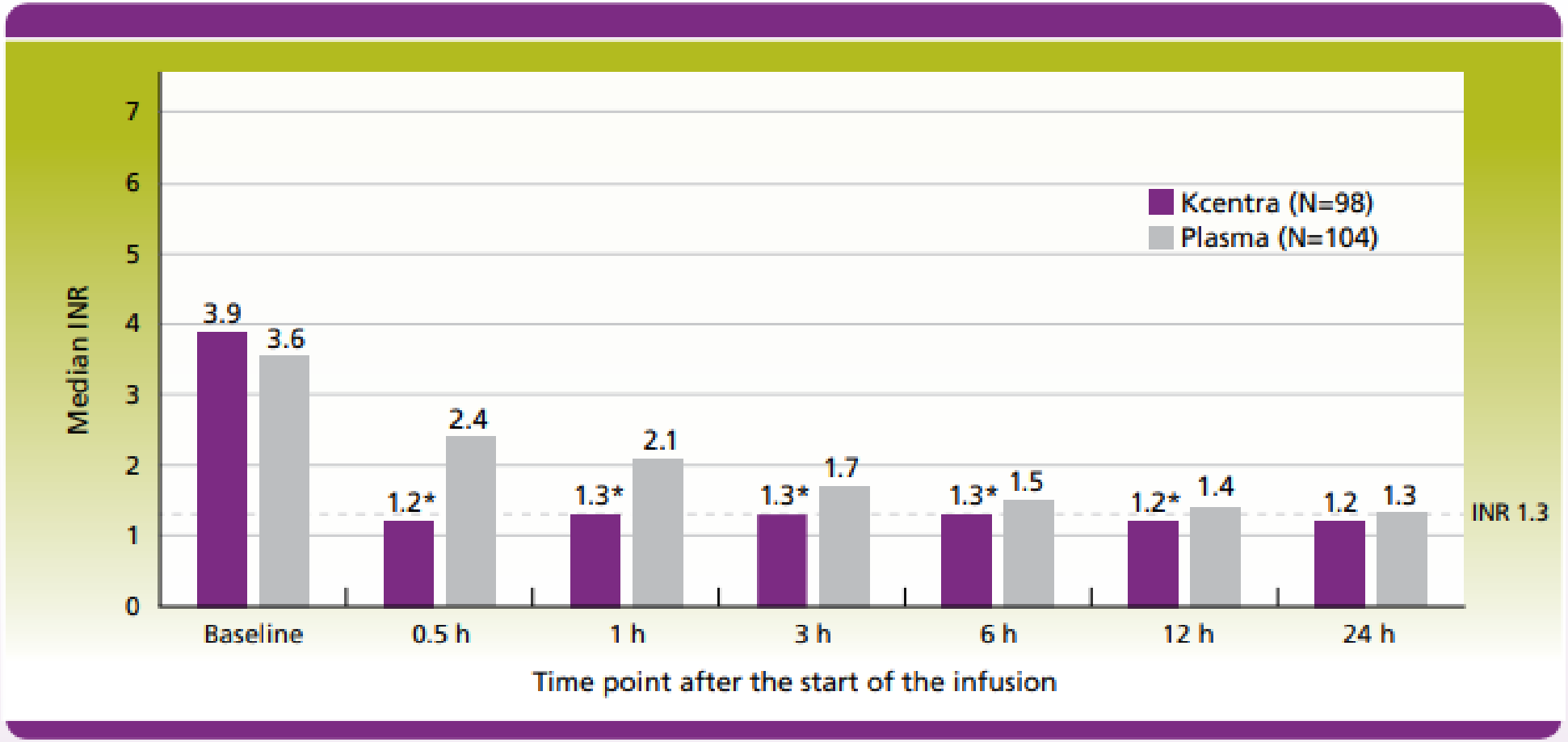
College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

Warfarin Reversal

Product	Time to Peak Effect	Risk for Thrombosis?
Oral Vitamin K	24-48 hours	Minimal
IV Vitamin K	12 hours	Minimal
FFP	90 minutes	Minimal
Kcentra®	30 minutes	Yes

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.
Sarode R, Milling TJ, Refaai MA, et al. Efficacy and safety of a 4-factor prothrombin complex concentrate in patients on vitamin K antagonists presenting with major bleeding: a randomized, plasma-controlled, phase IIIb study. Circulation. 2013;128(11):1234-1243.

Warfarin Reversal



*Statistically significant difference compared to plasma by 2-sided Wilcoxon test.
INR = international normalized ratio.

Sarode R, Milling TJ, Refaai MA, et al. Efficacy and safety of a 4-factor prothrombin complex concentrate in patients on vitamin K antagonists presenting with major bleeding: a randomized, plasma-controlled, phase IIIb study. Circulation. 2013;128(11):1234-1243.

Patient Case: MS

MS is a 64-year-old female with a past medical history of hypertension, coronary artery disease, and non-valvular atrial fibrillation who presents to Coumadin Clinic to have her weekly INR drawn. She states that she has not eaten any salads this week like she usually does, but that she has not had any unusual bruising or bleeding. She has not started any new medications recently, but she did take a few B.C. Powders this week when she had an “unbearable migraine that lasted for three days”.

Patient Case: MS

- Her home warfarin regimen is as follows:
  - 5 mg on Mondays, Wednesdays, and Fridays
  - 2.5 mg on Sundays, Tuesdays, Thursdays, and Saturdays

- You draw her INR with your point-of-care testing device and find that it is 6.4.

Patient Case: MS

1. Name three factors that could have contributed to an increased INR and an increased risk of bleeding in MS.

2. What other lab values or monitoring parameters would you order?

4. What would you recommend as the next course of action?
   a. Hold 1-2 doses of warfarin, then decrease her weekly dose
   b. Administer Kcentra®
   c. Switch her to Pradaxa®, as it has less bleeding than warfarin
   d. Administer SUBQ vitamin K

Oral Direct Thrombin Inhibitor: Dabigatran

http://levenstenlawfirm.com/wp-content/uploads/2012/04/pradaxa_lawyer.png

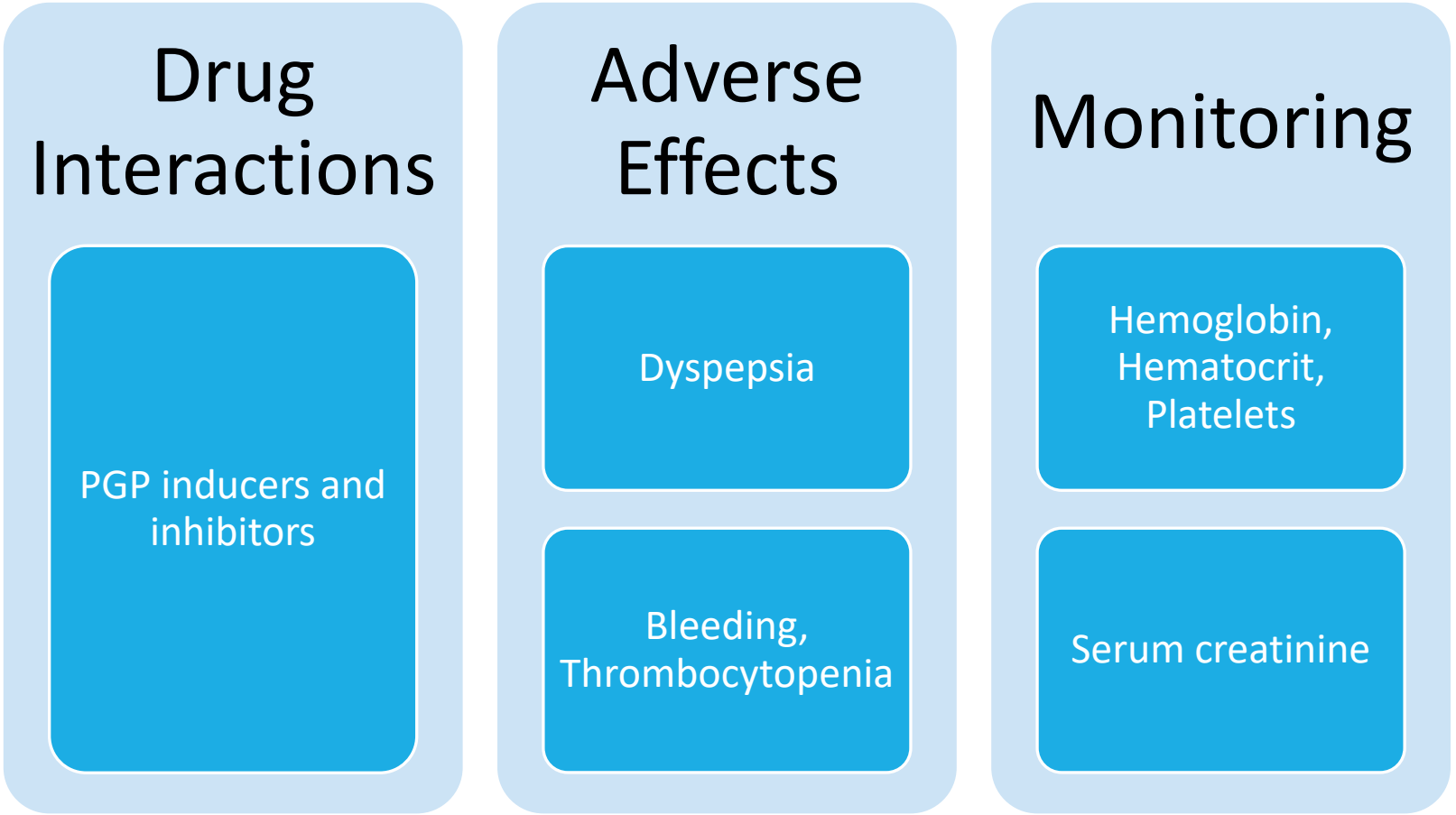
Dabigatran (Pradaxa®)

- Oral direct thrombin inhibitor
- Keep in original packaging

Indication	CrCl>30 ml/min	CrCl 15-30 ml/min
Non-valvular Atrial Fibrillation	150 mg twice daily	75 mg twice daily
Treatment of DVT/PE	150 mg twice daily after 5-10 days of IV anticoagulation	Not indicated
DVT/PE Secondary Prevention	150 mg twice daily	Not indicated
DVT/PE prophylaxis after hip replacement	110 mg once daily on day one, then 220 mg once daily	Not indicated

Available at: http://docs.boehringer-ingelheim.com/Prescribing Information/PIs/Pradaxa/Pradaxa. Accessed June 23, 2016.

Dabigatran (Pradaxa®)



Available at: http://docs.boehringer-ingelheim.com/Prescribing Information/PIs/Pradaxa/Pradaxa. Accessed June 23, 2016.

Dabigatran Reversal

- **Mild bleeding**
  - Discontinue dabigatran
  - Monitor hemoglobin and hematocrit

- **Life threatening or uncontrollable bleeding**
  - Discontinue dabigatran
  - Blood or factor products
    - Packed red blood cells
    - FFP ONLY if the patient has an underlying coagulopathy
  - **Idarucizumab (Praxbind®)**

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.
Available at: http://docs.boehringer-ingelheim.com/Prescribing Information/PIs/Pradaxa/Pradaxa. Accessed December 5, 2016.
Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

Idarucizumab (Praxbind®)

- Mechanism of action
  - Monoclonal antibody that binds and inactivates both bound and free dabigatran
- Onset of action: ~10 minutes
- Duration of action: 24 hours
- Indications
  - Emergent surgery
  - Life-threatening or uncontrollable bleeding

Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl. Accessed August 18, 2016.

https://www.praxbind.com/img/dosing-prep-bottles.jpg

Idarucizumab (Praxbind®)

- Dose
  - Two 2.5 g doses administered intravenously ≤15 minutes apart
  - May consider a second 5 g dose if bleeding does not resolve, or if a second emergent surgery is required
- Average wholesale price
  - $2100 per vial (2.5 g/50mL)
  - $4200 per dose

Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl. Accessed August 18, 2016.
N Engl J Med. 2015;373(6):511-20.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Idarucizumab for Dabigatran Reversal

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.

- Study objective
  - To examine the safety and efficacy of idarucizumab for the reversal of dabigatran in patients with serious bleeding, or who require urgent surgery
- Study design
  - Prospective cohort analysis

Idarucizumab for Dabigatran Reversal

- Inclusion criteria
  - Patients ≥18 years old on dabigatran
  - Group A:
    - Uncontrollable or life-threatening bleeding
    - Clinician determined that they required a reversal agent
  - Group B:
    - Required emergent surgery in ≤8 hours
- Intervention
  - 5 g intravenous idarucizumab
  - Given as two 2.5 g bolus infusions, administered <15 minutes apart

N Engl J Med. 2015;373(6):511-20.

Idarucizumab for Dabigatran Reversal

- Study population
  - Mean age 76.5 years old
  - Mean CrCl 58 ml/min
  - Median time since the last dose of dabigatran 15.4 hours
  - 96% were on dabigatran for atrial fibrillation

Type of bleeding in Group A	%
Gastrointestinal	39%
Intracranial	35%
Trauma	18%
Other	22%

Idarucizumab for Dabigatran Reversal

- Primary Endpoint
  - Maximum percent reversal
  - Calculation based on dilute thrombin time and ecarin clotting time

- Results
  - **Group A:** time to bleeding cessation was estimated to be about 11.4 hours

  - **Group B:** Normal hemostasis reported in 92% of patients

N Engl J Med. 2015;373(6):511-20.

Patient Case: JZ

- 64-year-old male presenting to the Emergency Department with dizziness and reporting dark tarry stool

- Past Medical History
  - Hypertension
  - Atrial fibrillation
  - Hyperlipidemia

- Home Medications
  - **Aspirin 81 mg once daily**
  - Lisinopril 20 mg once daily
  - Metoprolol tartrate 25 mg twice daily
  - Atorvastatin 20 mg once daily
  - **Dabigatran 150 mg twice daily**

- Vital Signs
  - Blood pressure 85/50
  - Heart rate 125
  - Temperature 36.4 degrees Celsius

- Laboratory Data
  - Serum creatinine 1.1 mg/dL
  - Hemoglobin 7.4
  - Hematocrit 26
  - All other labs within normal limits

Patient Case: JZ

1. If you were a member of the multidisciplinary treatment team, what would you recommend for the immediate treatment of JZ's upper GI bleed?

2. How would you recommend the nurse to administer the treatment?

3. What would you recommend monitoring during and after administration of the treatment?

Direct Oral Xa Inhibitors (DOACs)

APIXABAN, EDOXABAN, RIVAROXABAN

Apixaban (Eliquis®)

- Oral factor Xa inhibitor
- Indicated for stroke and systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation, as well as DVT and PE treatment
- Dosing:
  - 5 mg twice daily
  - 2.5 mg twice daily (adjusted)
- Dose adjustment in patients with two of the following when used for atrial fibrillation:
  - Age ≥80 years
  - Weight ≤60 kg
  - Serum creatinine ≥1.5 mg/dL

Eliquis [package insert] Princeton, NJ: Bristol-Myers Squibb; 2019.

http://drugsdetails.com/wp-content/uploads/2016/05/eliq-320x381.jpg

Edoxaban (Savaysa®)

- Oral factor Xa inhibitor

- Contraindicated for use in patients with non-valvular atrial fibrillation and a CrCl >95 ml/min

Indication	CrCl>50 ml/min	CrCl 15-50 ml/min
Non-valvular Atrial Fibrillation	60 mg once daily	30 mg once daily
Treatment of DVT/PE	60 mg once daily after 5-10 days of IV anticoagulation	30 mg once daily *also for patients <60 kg

Savaysa [prescribing information] Basking Ridge, NJ: Daiichi Sankyo, Inc. 2021.
tp://www.prestoimages.net/store20/rd648/648_pd2227643_1.png

Rivaroxaban (Xarelto®)

- Oral factor Xa inhibitor

- Counsel patients to take with the evening meal

Indication	CrCl>50 ml/min	CrCl 15-50 ml/min
Non-valvular Atrial Fibrillation	20 mg once daily	15 mg once daily
DVT/PE prophylaxis after hip or knee replacement	10 mg once daily	Not indicated
DVT/PE Treatment	15 mg twice daily for 21 days, followed by 20 mg daily	
Coronary artery disease or peripheral artery disease	2.5 mg twice daily	

Xarelto [package insert] Titusville, NJ: Janssen Pharmaceuticals, Inc; 2020.
https://attorneygroup.com/wp-content/uploads/2014/07/Xarelto-Side-Effects.jpg

DOAC Reversal

- **Emergent, life-threatening bleeding**
  - **Stop Xa inhibitor**
  - Andexanet Alfa (Andexxa®)
  - 4-Factor PCC (Kcentra ®): **Off-label use**
    - Weight based dosing
    - Fixed dosing

Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo) [prescribing information]. South San Francisco, CA: Portola Pharmaceuticals, Inc. 2018.
College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S
https://thesocialmedwork.com/andexxa-coagulation-factor-xa-recombinant-inactivated-zhzo.

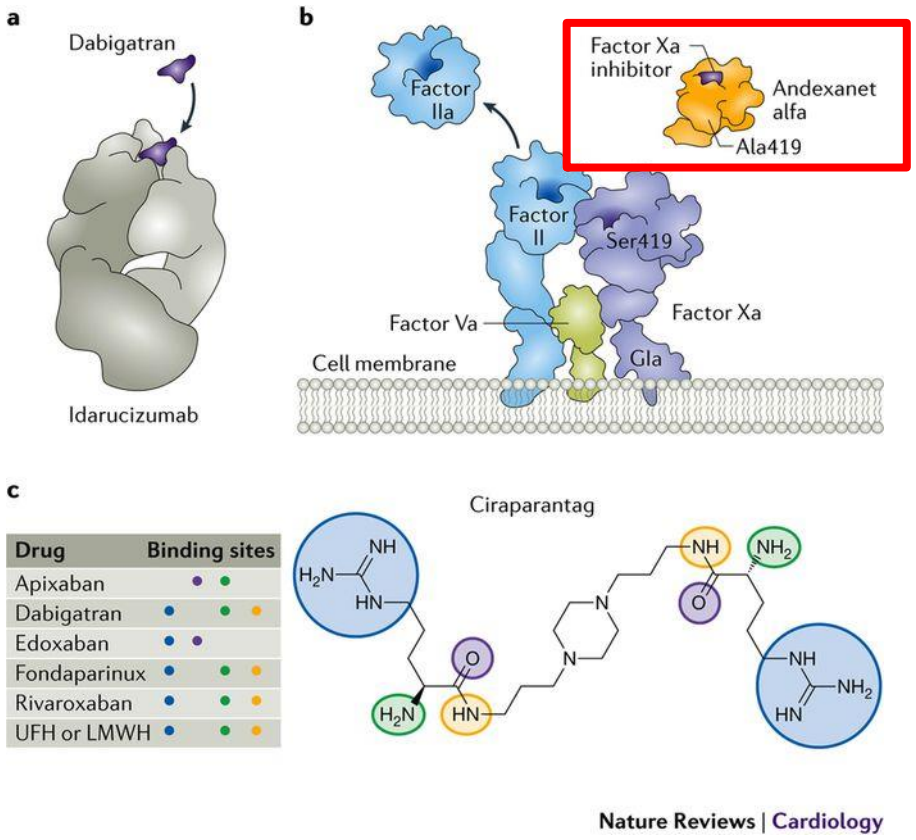
DOAC Reversal: Current Guideline Recommendations

Guideline	Recommendation
2019 AHA/ACC/HRS Focused Update of the Guideline for the Management of Patients with Atrial Fibrillation	"Andexanet alfa can be useful for the reversal of rivaroxaban and apixaban in the event of life-threatening or uncontrolled bleeding" **(Class IIa recommendation)**
American Society of Hematology 2018 Guidelines for the Management of VTE	"For patients with life-threatening bleeding during oral direct Xa inhibitor treatment of VTE, the ASH guideline panel suggests using either 4-factor PCC administration as an addition to cessation of DOAC or cessation or DOAC alone. No data are available comparing the efficacy of 4-factor PCC and andexanet alfa" **(Conditional recommendation)**
2012 Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report	"Give a NOAC-specific reversal agent or PCC if reversal agent not available"

January CT, et al. Heart Rhythm. 2019.
Gregory YH, et al. CHEST Journal. 2018.
Witt DM, et al. Blood Adv. 2018.

Andexanet alfa (Andexxa®)

- Recombinant human factor Xa that competitively binds factor Xa inhibitors and is catalytically inactive
- Competes with factor Xa for binding to tissue factor pathway inhibitor



Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo) [prescribing information]. South San Francisco, CA: Portola Pharmaceuticals, Inc. 2018.

Andexanet alfa (Andexxa®)

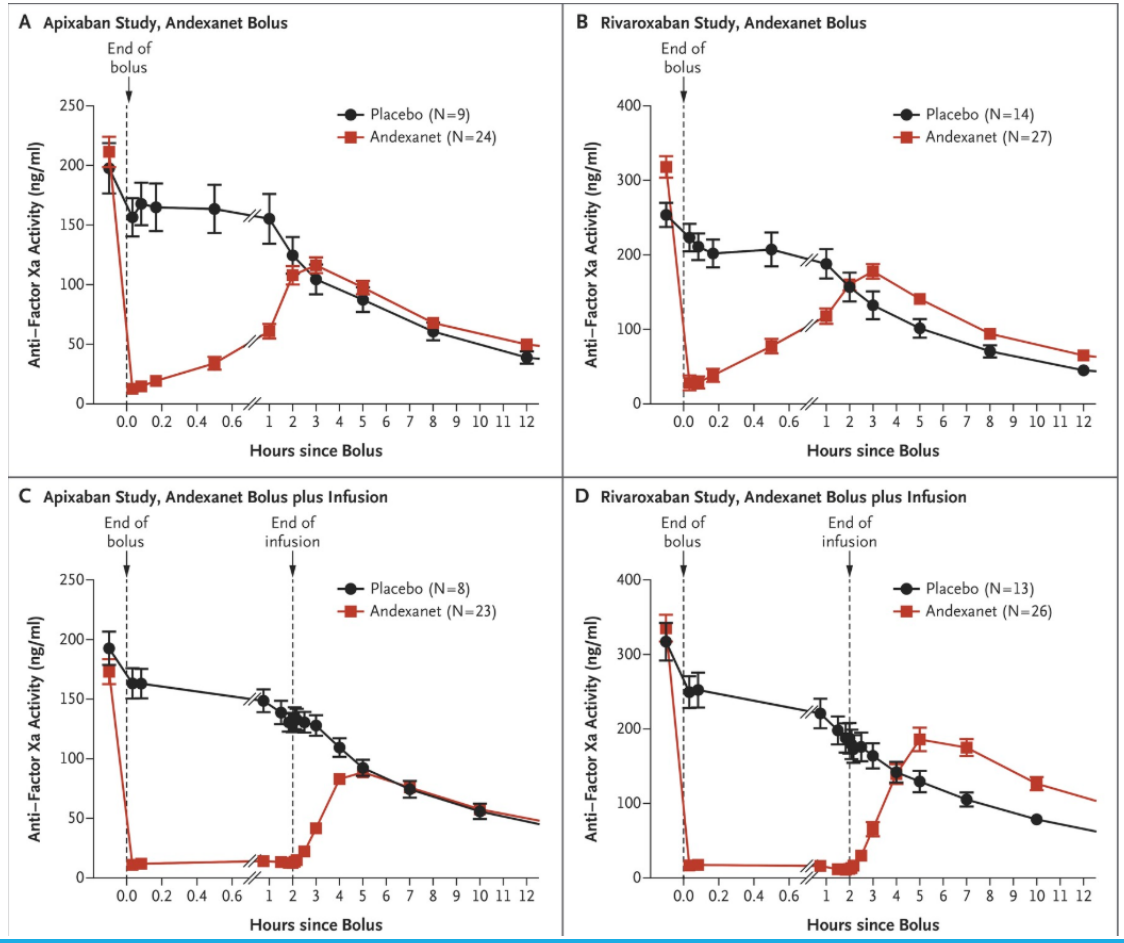
- Onset: ≤5 minutes
- Duration: 1-2 hours
- Boxed warning:
  - Thromboembolic risk, ischemic risk, cardiac arrest and sudden death

Anti-Xa inhibitor Dosing	Andexanet alfa Dosing
Apixaban ≤5 mg per day rivaroxaban ≤ 10 mg per day Apixaban OR rivaroxaban at any dose >8 hours before presentation	400 mg bolus 4 mg/min continuous infusion for 120 minutes
Apixaban >5 mg per day OR rivaroxaban >10 mg per day ≤8 hours before presentation	800 mg bolus 8 mg/min continuous infusion for 120 minutes

Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo) [prescribing information]. South San Francisco, CA: Portola Pharmaceuticals, Inc. 2018.

Andexanet alfa (Andexxa®)

- **Conditionally FDA-Approved** for patients treated with **rivaroxaban or apixaban**, when reversal is needed due to life-threatening or uncontrolled bleeding
  - Accelerated approval based on change from baseline in anti-Xa activity in healthy volunteers
  - **Improvement in hemostasis has not been established,** and continued approval for this indication may be contingent upon results of additional studies



Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo) [prescribing information]. South San Francisco, CA: Portola Pharmaceuticals, Inc. 2018.
Connolly SJ, Milling TJ, Eikelboom JW, et al. Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016;

ORIGINAL ARTICLE

Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

- Multicenter, open-label, single-group study
  - Safety and efficacy analysis
- Included patients on rivaroxaban or apixaban experiencing major, life-threatening bleeding
- Patients received a bolus plus a two-hour infusion of andexanet alfa

Anti-Xa inhibitor last taken	Andexanet alfa dose
>7 hours before presentation	400 mg bolus 480 mg continuous infusion
≤7 hours before presentation	800 mg bolus 960 mg continuous infusion

Connolly SJ, Milling TJ, Eikelboom JW, et al. Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016;

ORIGINAL ARTICLE

Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

- **Efficacy Results**
  - Rivaroxaban
    - Median anti-factor Xa activity decreased by 89% 12 hours after the infusion
  - Apixaban
    - Median anti-factor Xa activity decreased by 93% 12 hours after the infusion

- **Safety Results**
  - 12 patients had thromboembolic events (18%)
  - 10 patients died (15%)
    - 6 due to cardiovascular causes
    - 4 due to non-cardiovascular causes

Connolly SJ, Milling TJ, Eikelboom JW, et al. Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016;

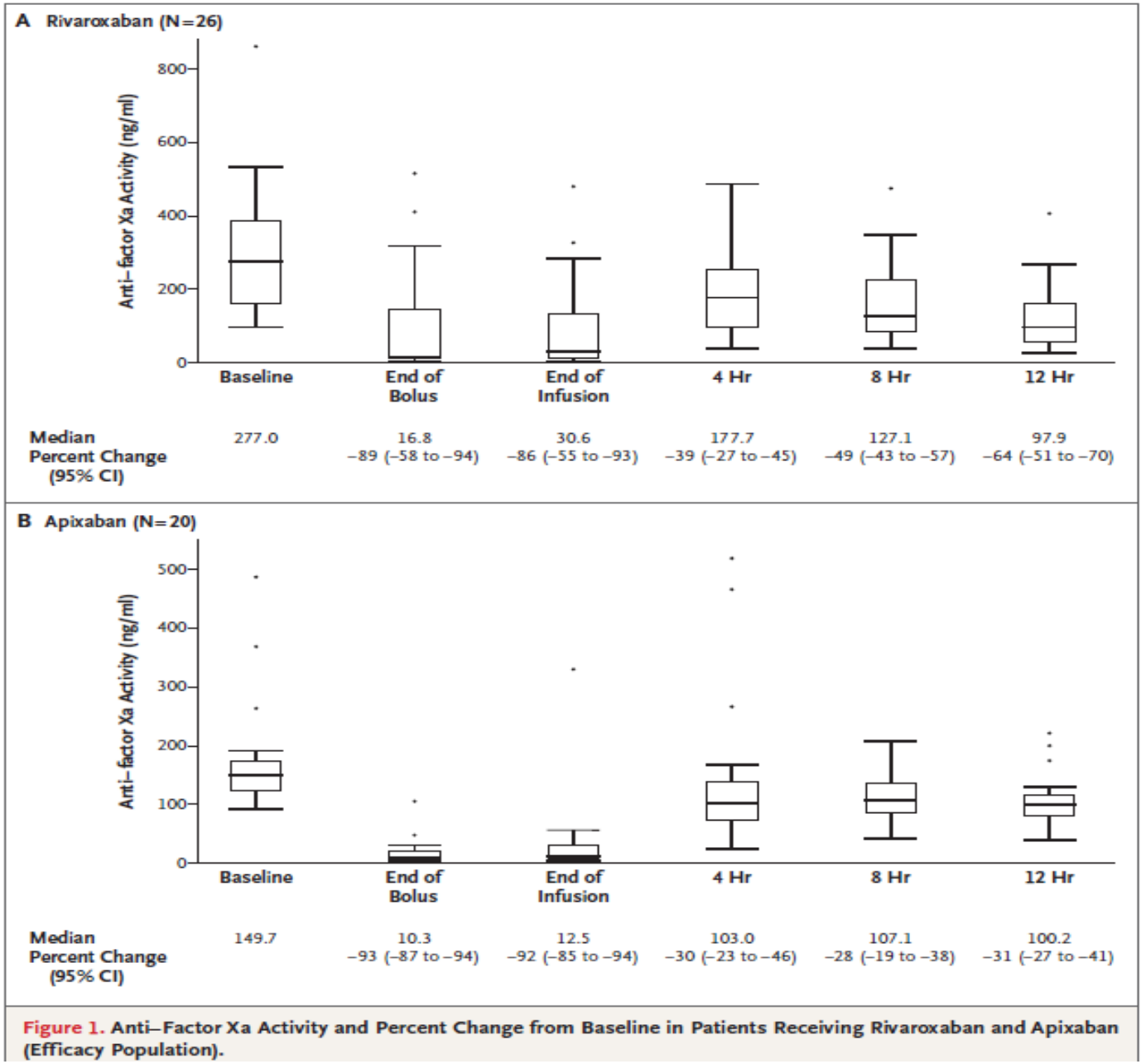


Figure 1. Anti–Factor Xa Activity and Percent Change from Baseline in Patients Receiving Rivaroxaban and Apixaban (Efficacy Population).

Connolly SJ, Milling TJ, Eikelboom JW, et al. Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors. N Engl J Med. 2016;

ANNEXA-4 trial

Design

- Multicenter, prospective, single-arm observational trial

Inclusion

- 352 patients with acute major bleeding

Primary Outcome

- % change in anti-factor Xa activity
- % of patients with excellent or good hemostatic efficacy at 12 hours

N Engl J Med. 2019. Apr 4;380(14): 1326-1335.

ANNEXA-4 trial

Results

- Median anti-factor Xa activity
  - Apixaban (92% reduction)
  - Rivaroxaban (92% reduction)
- Excellent or good hemostasis occurred (82%)

Adverse Effects

- Within 30 days, death occurred in 49 patients (14%) and 34 patients experienced a thrombotic event (10%)

N Engl J Med. 2019. Apr 4;380(14): 1326-1335.

Patient Case: SM

- 44-year-old female presenting with a ruptured abdominal aortic aneurysm, requiring emergent surgery

- Past Medical History:
  - Stable abdominal aortic aneurysm
  - Hypertension
  - Hyperlipidemia

- Home medications:
  - Metoprolol succinate 50 mg once daily
  - Atorvastatin 20 mg once daily
  - ASA 81 mg once daily
  - Losartan 25 mg once daily
  - **Rivaroxaban 20 mg once daily**

- Pertinent laboratory data:
  - Hgb 7.1
  - Hct 24
  - Platelets 274
  - Blood pressure 71/36 mm Hg
  - Scr 0.8 mg/dL
  - All other labs within normal limits

Patient Case: SM

1. The surgeon turns to you to reverse the rivaroxaban prior to surgery. What treatment do you recommend?

2. What will you monitor (labs, physical exam, etc.) for your chosen reversal method?

Take Home Points

- Be aware of institutional formulary reversal products
  - Does your institution have Andexxa®? If so, what restriction criteria are in place for use?
- Institute standardized reversal guidelines for life-threatening bleeding and emergent surgeries, if not already in place
- Update standardized reversal guidelines regularly and maintain them in an easy to access location

References

American Society of Hematology

- Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances*. 2018;2(22):3257-3291.

American College of Chest Physicians

- College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e44S-88S.

American College of Cardiology

- Tomaselli GF, Mahaffey KW, Cuker A, Dobesh PP, Doherty JU, Eikelboom JW, Florido R, Gluckman TJ, Hucker W, Mehran R, Messé SR, Perino AC, Rodriguez F, Sarode R, Siegal D, Wiggins BS. 2020 ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2020 Aug, 76(5) 594-622. doi:10.1016/j.jacc.2020.04.053

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