# Hemorrhagic Stroke Related to Anticoagulation



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## Hemorrhagic stroke

- » Second important cause of stroke after ischemic stroke. Incidence of 13%
- » Caused by weakened vessel that ruptures and bleeds into the surrounding brain
- » Blood accumulates and compresses the surrounding brain tissue
- » Overall incidence of ICH ranges from 12 to 31 per 100,000 people
- » ICH is highest in Asians followed by blacks and least in whites



## **Hemorrhagic Stroke**

- » Intracerebral hemorrhage
  - Bleeding derived from arterioles or small arteries
  - Localized hematoma spreading along white matter pathways
  - Common causes
    - Hypertension, trauma, Bleeding diatheses, amyloid angiopathy, drug use (amphetamines and cocaine), vascular malformations, tumors, aneurysmal rupture and vasculitis
- » Subarachnoid hemorrhage
  - Rupture of the arterial aneurysms is the major cause
  - Other causes include vascular malformations, bleeding diatheses, trauma, amyloid, drug use
  - Bleeding is less abrupt and may continue over a long time

## Hemorrhagic stroke

- » ICH is the serious complication of oral anticoagulant therapy with mortality of more than 50%
- » Decision to administer anticoagulant is based on the risk of thrombosis and its complication greater than risk of bleeding and its complication.



## **Anticoagulant therapy**

- » Direct oral anticoagulants (DOACs)
  - Rivaroxaban, apixaban, edoxaban and dabigatran
- » Heparins (low molecular weight, Heparin and fondaparinux)
- » Warfarin or vitamin K antagonists
- » Antiplatelet therapy



## Pathogenesis of Anticoagulant Associated Bleeding

- » Loss of vascular integrity
  - Anticoagulant interferes with normal hemostatic process that resolves microscopic bleeding events leading to hematoma expansion
  - Breaches of vascular integrity may be mechanical (trauma, tumor invasion, thrombosis or hypertension)
    - Altered endothelial barrier function (sepsis, ischemia, certain chemotherapeutic drugs or biologics)
- » Microbleeds and other subclinical bleeding events
  - Hypertension, amyloid angiopathy, COPD, cigarette smoking, trauma, dementia, diabetes and normal aging



## **Annual Incidence of Intracranial Hemorrhage In Elderly Adults Not Taking Warfarin**

Study	Year published	Population characteristics	Age	Population (n)	Intracranial bleeds (%/year)
			20-64	409,193	0.051
Krishnamurthi et al <sup>10</sup>	2013	General population, high income	65-74	273,711	0.25
			≥75	364,687	0.38
			<65	12,748	0.31
Friberg et al <sup>11</sup> 200	2009	AF Swedish patients, never used warfarin	65-74	13,317	0.65
			≥75	64,641	0.67
			<65	3 263 (~75)	0.10
Singer et al <sup>12</sup>	2000	AF patients not	65-74	65-74	0.12
	2009	receiving warfarin	75-84	3 000(~75)	0.43
			≥85	3,090(>73)	0.79
Shen et al <sup>13</sup>	2007	2007 AF patients not receiving warfarin	<75	22,682	0.09
	2007		≥75	16,343	0.23



## Intracranial hemorrhage Among Patients Taking Newer Anticoagulants

Intracranial bleeds ITT (%/year)	Events	Population (n)	Trial	Drug and dosage
0.30	36	6076	RE-LY <sup>16</sup>	Dabigatran 150 mg bid
0.23	27	6015	RE-LY <sup>16</sup>	Dabigatran 110 mg bid
0.57	67	7131	ROCKET-AF <sup>17</sup>	Rivaroxaban 20 mg od
0.33	52	9120	ARISTOTLE <sup>18</sup>	Apixaban 5/2.5 mg bid
0.39	61	7035	ENGAGE AF <sup>19</sup>	Edoxaban 60/30 mg qd
0.26	41	7034	ENGAGE AF <sup>19</sup>	Edoxaban 30/15 mg qd

### Intracranial Hemorrhage Among Patients Taking Oral Anticoagulants

- » ICH in patients taking VKA is between 0.3% 0.6% and in DOAC it is 0.1%-0.2%
- » DOACs are associated 50% less ICH compared to VKA



## **Tests To Determine The Reversibility**

- » Routine tests are less useful for measuring the anticoagulant effects of DOACs
- » Dabigatran has the greatest effect on aPTT
- » Rivaroxaban, apixaban and edoxaban has greater effect on PT than aPTT
- » Thrombin time is the most sensitive test for dabigatran. However it is prolonged even with lowest concentration of dabigatran
- » Diluted thrombin time (diluting the plasma 8 fold with control plasma before adding thrombin) is used to overcome the dabigatran effect and calibration curve will tell us the concentration of dabigatran
- Reversal should be considered if the dabigatran concentration exceeds 30ng/ml (lower limit of quantification of the assay)

## **Tests to determine the reversibility**

- » Anti-factor Xa assays are used to quantify plasma levels of rivaroxaban, apixaban or edoxaban
- » Comparing the standard curves constructed with known concentration of these drugs will help in quantifying drug level
- » Reversal should be considered if drug levels exceed 30ng/ml
- » No reversal is needed if the plasma concentration of dabigatran is < or equal to 30 ng/ml or aPTT ration is < 1.2</p>
- » For rivaroxaban concentration of <30 ng/ml or PT ratio using sensitive reagent is <1.2 no reversal is needed</p>



### **Reversal of OACs**

Suggested dose	Mechanism of action	Target substance	Active component
400mg – 800mg IV bolus followed by infusion of 480mg- 900mg depending on the type of agents	Recombinant factor Xa that competes with native factor Xa for binding of rivoraxaban etc, heparin,LMWH and fondaparinaux-antithrombin III complex	Factor Xa inhibitors, heparin, LMWH and fondaparinaux	Andexanet alfa
5g IV bolus	Noncompetitive , specific and direct binding of dabigatran	Dabigatran	Idarucizumab
25-50 U/kg IV	Replacement of factor II, IX,X, VII ( 4 factor), protein C, S and Z in some products	Vitamin K antagonists	3 or 4 factor PCC
300mg bolus	Charge dependent hydrogen bonding to all	Universal antidote	Aripazine, ciraparantag





Anticoagulant-Associated Intracranial Hemorrhage in the Era of Reversal Agents, Volume: 48, Issue: 5, Pages: 1432-1437, DOI: (10.1161/STROKEAHA.116.013343)



## Anticoagulation Resumption After Intracranial hemorrhage

- » Anticoagulation is supported by class I guidelines for patients with A Fib, high risk of ischemic stroke, systemic embolism, mechanical prosthetic valve or those who are at risk for VTE or PE
- » ICH patients are excluded from studies for stroke prevention in AF
- » Need to carefully balance the risk of bleeding and thromboembolism
- » No guidelines to restart the anticoagulation
- » Review article anticoagulation resumption after ICH by Yuan gang and Gregory Y Lip published in current atherosclerosis reports 2018, gives simplistic steps for such patients







## **Risk of Recurrent ICH After OAC Resumption**

- » 1 year recurrent ICH in nonanticoagulated patients ranges from 0-8.6%
- » In patients resuming the OAC it is 2.5-8%
- » In majority of studies the OAC did not increase the risk of recurrent ICH



# Association between resuming anticoagulants and thromboembolic complications



Restarting Anticoagulant Therapy After Intracranial Hemorrhage, Volume: 48, Issue: 6, Pages: 1594-1600, DOI: (10.1161/STROKEAHA.116.016327)

# Association between resuming anticoagulants and ICH recurrence

Study -		1		Risk ratio (95% CI)	% Weigh
Anti	coagulants	No An	ticoagulants		
Gathier				3.23 (0.14,72.46)	0.2
Claassen				_ 3.25 (0.14,76.01)	0.2
Nielsen				0.50 (0.34,0.73)	36.7
Majeed		-		1.55 (0.66,3.64)	3.5
Kuramatsu	_			1.24 (0.68,2.24)	8.8
De Vleeschouwer				0.46 (0.06,3.58)	1.7
Ottosen				1.54 (1.18,2.01)	39.4
Yung	_			1.02 (0.57,1.84)	9.4
Overall (95% CI)		\$		1.01 (0.58, 1.77)	
-	.1	1	10 Risk ratio	_	

- 8 studies were included
- 5036 patients with ICH
- 1899 (35.8%) were on anticoagulation followup of 3494 person years
- Anticoagulation not started in 3407 (64%) followed for 7030 person years
- Recurrence of ICH events was seen in 166 (8.7%) vs 267 (7.8%)
- No difference between
  the two groups

Restarting Anticoagulant Therapy After Intracranial Hemorrhage, Volume: 48, Issue: 6, Pages: 1594-1600, DOI: (10.1161/STROKEAHA.116.016327)



## **Limitations of the Review**

- » Lack of data on the volume of hematoma
  - Not sure whether the hematoma was small in patients who resumed the anticoagulation
- » None of the studies gave the location of the hematoma
  - Lobar hematomas are likely related to amyloid angiopathy which has higher rate of recurrence 22% compared to deep cortical location 4%
- » All the studies in the review had VKA as the medication of choice
- » Newer OAC have lower rate of ICH
- » Subdural has higher recurrence rate (12%) vs ICH (2%)
- Clinical factors (BP control, kidney function, liver function, labile INR, Diabetes) were unknown



## **Risk Factors for Recurrent ICH**

- Large area ICH, ICH history, lobar ICH location, cerebral microbleeds, amyloid angiopathy, AV malformations, cerebral aneurysm, lacunar infarcts, Asian population
- » Modifiable risk factors
  - Alcohol, tobacco, risk of fall
  - Uncontrolled hypertension, Diabetes



## Risk Scores for Evaluating Anticoagulated Individual's Risk of Bleeding

- » Several scores are proposed
  - mOBRI (modified outpatients bleeding risk index)
    - Age >65, previous stroke, GI bleed, > or- 1 of comorbidities (recent MI, hematocrit of < 30%, creatinine >1.5 mg, diabetes)
    - Low risk 0, Intermediate risk 1-2 score, High risk 3 or more
  - HEMORR2HAGES (hepatic or renal disease, ethanol abuse, malignancy, age >75, reduced platelet or function, re-bleeding risk, hypertension, anemia, genetic factor, excessive fall risk, stroke)
    - Prior bleed 2 points, rest of the factors each have point of 1
    - Low risk 0-1, Intermediate risk 2-3, High risk 4 or more
  - These scores are used to identify patients at risk for bleeding for careful review and follow up and not considered as absolute contraindications
  - These scores should not be used to withhold anticoagulation as patients at risk for thromboembolism have increased mortality

### **Risk Scores for Evaluating Risk of Thromboembolism**

- » CHA2DS2-VASc Atrial fibrillation patients
  - CHF, HTN, age > 75 (2 pts), Diabetes, Prior Stroke/TIA/Thromboembolism, Vascular disease (previous MI, PAD or aortic plaque), Age 65-74, Sex category (female gender)
  - Risk of stroke annually ranges from 1.3% pver 15%)
  - Low risk 0-1, intermediate 2-3 and high risk 4 or more
- » Modified wells score –DVT/PE
  - Active cancer, immobilization, recent bedridden, tenderness along the deep venous system, entire leg swollen, calf swelling, pitting edema, collateral superficial vein
  - Low risk 0, intermediate risk 1-2, high risk 3 or more
- » Meta-analysis about OAC resumption after ICH , reinitiation reduced thromboembolic complications (HR 0.34)
  - Murthy et al 2017 stroke
- » MUCH- Italy study (multicenter study on cerebral hemorrhage) showed 81% reduced risk of thromboembolism among patients restarting OAC after ICH.
  - Pole et al 2018 Thrombo Haemost

## **OAC Resumption After ICH**

- » Large proportion do not restart the anticoagulation
- Older studies have shown OAC can be safely withheld for certain period of time without high risk of thromboembolism ( one study had withheld for 506 days )
- » Duration of withholding is uncertain
- » In Reversal-AD study (reversal of dabigatran by Idarucizumab) majority of thrombotic event occurred within 30 days after ICH



## **Timing of Restarting OAC**

- » Opinion ranges from 3 days to 30 weeks for warfarin
- » Danish nationwide cohort (n=1725) OAC was restarted after 2-4 weeks of ICH
- » In multicenter retrospective study in Germany (n=719)
  - Anticoagulation restarted at median of 31 days
  - Fewer ischemic events (5.2 vs 15) and similar hemorrhagic complications (8.1 vs 6.6) were observed in anticoagulated patients compared to no OAC
    - Kuramatsu et al JAMA 2015
  - Another study demonstrated that OAC resumption at 2 weeks after ICH resulted in less clinical events including thromboembolism
    - Park YA et al Heart rhythm 2016
- » OAC should be avoided in the first 2 weeks after OAC associated parenchymal ICH

## **Timing of Restarting OAC**

- » Timing depends on individual clinical condition
  - Ex In brainstem or cerebellar ICH timing should be delayed at least 8-10 weeks after the event
  - Whereas in prosthetic heart valve patients the OAC should be resumed at 2 weeks based on thromboembolic risk or sooner if the bleed is small and causative mechanism is stabilized
  - Brain CT or MRI will help to confirm resolution of ICH
- » NOACs have lower risk of ICH and bleeding is also less severe, smaller hematoma volumes, less expansion and lower risk of poor functional outcome or death
- » Heparin is used as temporary parenteral anticoagulant. Low dose heparin can be started after 48 hours of onset of ICH without increased hematoma growth and should be used for DVT/PE prophylaxis
  - Orkern DN et al Neurologist 2009



## Reducing the Risk of Recurrent ICH After Restarting OAC

- » Control the modifiable risk factors (Tobacco, alcohol, risk of all, Hypertension, liver disease etc)
- » In patients OAC is not an option, L atrial appendage occlusion in patients with AF and IVC filter in patients with DVT or PE
- In patients treated with warfarin (mechanical valve) controlling the INR ( >70%) is important
- » Recommending lower INR than guideline should not be encouraged



## Anticoagulation Reversal Medication Guidance and Treatment Strategies

Presented By: Jason Sturgeon RPh Licking Memorial Health Systems



# **R**<sup>3</sup>**Report** Requirement, Rationale, Reference

A complimentary publication of <u>The Joint Commission</u> Issue 19, Dec. 7, 2018

### National Patient Safety Goal for anticoagulant therapy

<u>Effective July 1, 2019</u>, eight new elements of performance will be applicable to all Joint Commission-accredited hospitals, critical access hospitals, nursing care centers, and medical centers (accredited under the ambulatory health care program). These new requirements are at NPSG.03.05.01 in the "National Patient Safety Goals" chapter. For years, this NPSG has played an important role in improving the safety of patients receiving anticoagulation therapy. However, there has been a rise in adverse drug events associated with direct oral anticoagulants (DOACs), and The Joint Commission believes that relevant updates to this NPSG to address DOACs may help reverse that trend.



### **RESPONSE TO JOINT COMMISSION**

Revised inpatient guidelines and policies

- Initiation and maintenance of anticoagulation therapy
- Guidelines for reversal and management of bleeding events
- Perioperative management
- Baseline and ongoing lab monitoring
- Evaluate safety practices
- Education

Outpatient follow up

- Add DOAC's to Anticoagulation management in MTC
- Provide education, dose evaluation, evaluate compliance, lab monitoring (renal, liver, H&H)
- Refer new DOAC patients to MTC

#### TABLE 1

Indication	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
VTE treatment and prevention of recurrence	CrCl > 30 mL/min: 150 mg twice daily	15 mg twice daily with food for first 21 days for initial treatment of VTE, then 20 mg once daily with food <sup>a</sup>	<i>Treatment:</i> 10 mg twice daily for 7 days, followed by 5 mg twice daily <i>Prevention of recurrence:</i> 2.5 mg twice daily	VTE treatment only: 60 mg once daily <sup>b</sup> CrCl 15–50 mL/min, body weight ≤60 kg, or use of certain P-gp inhibitors <sup>c</sup> : 30 mg once daily
VTE prophylaxis	<i>CrCl &gt; 30 mL/min</i> <i>after hip replacement</i> <i>surgery:</i> 110 mg on first day, then 220 mg once daily	10 mg once daily with or without food after hip or knee replacement surgery <sup>a</sup>	2.5 mg twice daily after hip or knee replacement surgery	Not approved by FDA for this indication <sup>b</sup>
Stroke/systemic embolism prophylaxis in nonvalvular atrial fibrillation	<i>CrCl &gt; 30 mL/min:</i> 150 mg twice daily <i>CrCl 15–30 mL/min:</i> 75 mg twice daily	<i>CrCl &gt; 50 mL/min:</i> 20 mg once daily with evening meal <i>CrCl 15–50 mL/min:</i> 15 mg once daily with evening meal	5 mg twice daily, or 2.5 mg twice daily in patients with at least 2 of the following characteristics: age $\geq$ 80 yr, body weight $\leq$ 60 kg, or SCr $\geq$ 1.5 mg/dL	CrCl > 95 mL/min: do not use <sup>d</sup> CrCl > 50-95 mL/min: 60 mg once daily CrCl 15-50 mL/min: 30 mg once daily

#### Direct Oral Anticoagulant FDA-approved Indications and Dosing<sup>4-9</sup>

CrCl (using total body weight) = creatinine clearance, FDA = Food and Drug Administration, P-gp = P-glycoprotein, SCr = serum creatinine; VTE = venous thromboembolism

- <sup>a</sup> Rivaroxaban use for VTE treatment and prophylaxis should be avoided in patients with CrCl <30 mL/min because of an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population.
- <sup>b</sup> Edoxaban is approved by FDA for VTE treatment and stroke and systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation, but not for prevention of VTE recurrence or VTE prophylaxis.
- <sup>c</sup> In the Hokusai study of edoxaban, a reduced dosage of 30 mg once daily was used for patients receiving verapamil, quinidine, or short-term azithromycin, clarithromycin, erythromycin, oral itraconazole, or oral ketoconazole therapy.
- <sup>d</sup> Edoxaban should not be used for stroke or systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation and CrCl >95 mL/min because of an increased risk of ischemic stroke from edoxaban 60 mg once daily compared with warfarin in the ENGAGE AF-TIMI 48 study (Giugliano R et al. *N Engl J Med.* 2013; 369:2093-104).



### When should a DOAC not be the first choice?

- Pro-thrombotic states: e.g. cancer
- Severe renal impairment (CrCl < 15 ml/min)
- Moderate to severe hepatic impairment
- Clinically significant drug interactions
- Extremely high body weight (> 120 kg ?)
- Prohibitive cost





DOWNLOADED FROM www.DOACresources.org

MANAGING AND REVERSING DIRECT ORAL ANTICOAGULANTS | 3

### Major Bleeding: DOACs vs. Warfarin in NVAF



### Case Fatality Rate after Major Bleeding: Warfarin vs. DOACs

	Warfarin Major Bleeds/Fatal bleeds	New agent Major Bleeds/Fatal bleeds
ROCKET AF	386/55 <b>14%</b>	395/27 <b>7%</b>
Dabigatran systematic review	407/53* <b>13%</b>	627/57* <b>9.1%</b>
ARISTOTLE	462/55 <b>12%</b>	327/34 <b>10%</b>
ENGAGE-AF	524/59 <b>11.3%</b>	418/32 <b>7.7%</b>
Dresden Registry	N/A	5.1%

For more precise (and pooled) estimates, see:

Chai-Adisaksopha C, et al. J Thromb Haemost 2015; 13: 2012–20.

## Management of DOAC bleeding

- Assessment of anticoagulation status
  - Medication, dose, time since last dose, renal function
- Anticoagulation generally resolved after 5 half-lives since last dose
  - Dabigatran (3-5 days)
  - Rivaroxaban (1-2 days)
  - Apixaban (1.5-3 days)
  - Edoxaban (1.25-2 days)

## Hemorrhage Management

- Degree of hemorrhage
- Location of hemorrhage
- Timing of last dose of DOAC
- Hemodynamic stability
- Risk of thrombosis
- Normal PT/aPTT likely excludes significant effect of DOAC



## Reversal of Anticoagulants

- Immediately HOLD further doses of anticoagulant
- Investigate for the source of the bleed
- Supportive therapy
- Hemostasis measures
- Consider antidote only for emergent life threatening situations
  - Reversal generally unnecessary for elective interventions
  - May be necessary for emergent interventions
- Strategy depends on availability, cost, patient characteristics
- Transfusions
- Resume AC as soon as hemostasis achieved and benefit > risk

### **Management of NOAC-Related Bleeding**



			Severe/Life Threatening*	
	Mild	Moderate	Dabigatran	FXa Inhibitors
SUPPORTIVE MEASURES				
Delay or discontinue NOAC	×	Х	х	х
Discontinue (or reverse) other antithrombotics	х	Х	х	х
Decrease absorption-activated charcoal if last dose 2-4 h		Х	х	х
Maintain diuresis/volume support (fluids)		Х	х	х
Mechanical compression/intervention to establish hemostasis		Х	Х	х
Transfusion: PRBCs, FFP (as plasma expander), platelets		Х	Х	Х
Dialysis			X†	
NONSPECIFIC HEMOSTATIC AGENTS				
PCC > aPCC > rFVIIa				X‡
SPECIFIC REVERSAL AGENTS				
Idarucizumab			х	
Andexanet alfa				If approved



### **Correction of Coagulopathy**

### **Direct Thrombin Inhibitors (Dabigatran)**

Bivalent: Hirudin, Bivalirudin, Desirudin, Lepirudin Univalent: Argatroban

Mechanism: Directly inhibits the enzyme thrombin (factor II)

Treatment:

- -Ascertain time of last dose
- -If < 2 hrs since ingestion, administer activated charcoal
- -Reversal: idarucizumab (Praxbind) Adheres to thrombin binding sites
- -Administer PCC
- -Approx 50% dialyzable

Frontera, et al. Neurocritical Care, 24, 2016



### Idarucizumab: An Antidote to Dabigatran

### DEVELOPMENT

- Monoclonal mouse antibody with high dabigatran binding affinity
- Humanized & expressed as Fab fragment in hamster cells

#### PROPERTIES

- Binding affinity ~350 times higher than binding of dabigatran to thrombin
- No procoagulant or anticoagulant effects
- Short half life
  IV administration, immediate onset of action

#### EXPECTED LOW RISK OF ADVERSE REACTIONS

- No Fc receptor binding (cellular mediators of antibody functions)
- No endogenous targets

Glund S et al. AHA, Dallas, TX, USA, November 2013; Schiele F et al. Blood. 2013;121:3554-62







Pollack CV, et al. N Engl J Med. 2017;377:431-441.

![](_page_40_Figure_2.jpeg)

![](_page_41_Figure_0.jpeg)

Glund S et al. AHA 2013; abstract 17765

Healthy volunteer study: immediate, dose-dependent reversal of dabigatran anticoagulation

![](_page_41_Figure_3.jpeg)

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### **REVERSE AD Full cohort Study Results Overview**

Idarucizumab was 100% effective in reversing the anticoagulant effect of dabigatran:

- among 300 patients with uncontrolled bleeding (median time to bleeding cessation, 2.5 hours)
- and among 200 patients who required an urgent procedure (median time to procedure initiation, 1.6 hours).

Pollack CV N Engl J Med Volume 377(5):431-441 August 3, 2017

### **Correction of Coagulopathy**

### Direct Xa Inhibitors (Rivaroxaban, Apixaban, Edoxaban)

Mechanism: Inhibits factor Xa thereby interrupting the intrinsic and extrinsic pathway  $\rightarrow$  inhibits thrombin formation

Treatment:

- -Ascertain time of last dose
- -If < 2 hrs, administer 50 g activated charcoal
- -Prothrombin Complex Concentrate (PCC)
- -Reversal: Andexanet alfa may be a future option.

Frontera, et al. Neurocritical Care, 24, 2016

![](_page_43_Picture_9.jpeg)

### Cost of Andexanet Alfa vs PCC

- 95 kg patient on apixaban 5 mg BID presenting with intracranial hemorrhage; last dose 6 hours ago
- Andexanet alfa pricing: \$2,750/100 mg vial
  - Low dose (400 mg IV bolus + 4 mg/min IV infusion x 120 min) = 880 mg = 9 vials = \$2,750/100 mg vial x 9 vials = \$24,750
- Kcentra<sup>®</sup> pricing: \$1.54/IU
  - Dose (50 IU/kg)
    - \$1.54/IU x [(50 IU/kg) x 95 kg] = **\$7,315**
- Cost difference = \$17,435

### Reversal of Rivaroxaban and Dabigatran by PCC

![](_page_45_Figure_1.jpeg)

Eerenberg ES, et al. Circulation. 2011;124(14):1573-1579.

## KCENTRA (4 FACTOR PROTHROMBIN COMPLEX CONCENTRATE)

DOAC reversal (specifically Factor Xa Inhibitors)

- Dose: 50 units/kg IV x 1 dose (maximum dose 5000units)
- Infusion rate: 0.12 ml/kg/min up to a maximum rate of 8.4 ml/min
- Cost: \$1.54 / unit (Roughly \$4000 \$8000 / dose)

Vitamin K Antagonist reversal

Pretreatment INR	Dose	Maximum Dose
2 – 3.9	25 units / kg	2500 units
4 - 6	35 units / kg	3500 units
Greater than 6	50 units / kg	5000 units

HS 78 YOF presents to ED with ICH and last dose of dabigatran was 6 hours ago. CrCl 30 ml/min with a prolonged aPTT.

- A. FFP
- B. Kcentra (4 factor PCC)
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_47_Picture_7.jpeg)

HS 78 YOF presents to ED with ICH and last dose of dabigatran was 6 hours ago. CrCl 30 ml/min with a prolonged aPTT.

- A. FFP
- B. Kcentra (4 factor PCC)
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_48_Picture_7.jpeg)

TC 55 YOF presents to ED with moderate GIB and last dose of rivaroxaban 28 hours ago. Hx of CHF, normal PT, CrCl 95 ml/min, Hgb 8.1, BP 105 / 60.

- A. FFP
- B. Supportive measures and address hemodynamic stability
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_49_Picture_7.jpeg)

TC 55 YOF presents to ED with moderate GIB and last dose of rivaroxaban 28 hours ago. Hx of CHF, normal PT, CrCl 95 ml/min, Hgb 8.1, BP 105 / 60.

- B. Supportive measures and address hemodynamic stability
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_50_Picture_7.jpeg)

A. FFP

MP YOM presents to ED with ICH and last dose of apixaban 8 hours ago. CrCl 30 ml/min, prolonged PT.

- A. FFP
- B. Kcentra (4 factor PCC)
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_51_Picture_7.jpeg)

MP YOM presents to ED with ICH and last dose of apixaban 8 hours ago. CrCl 30 ml/min, prolonged PT.

What is the preferred reversal method of treatment?

A. FFP

- B. Kcentra (4 factor PCC)
- C. Idarucizumab (Praxbind)
- D. Phytonadione (Vitamin K)

![](_page_52_Picture_7.jpeg)