Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

Acute VTE Care Transition Order Set (Adult)

ACTION

Administration

Document Purpose

This order set may be used for adult patients diagnosed with venous thromboembolism (VTE: deep vein thrombosis, pulmonary embolism) who are ready to be transferred from the hospital or emergency department to outpatient care settings.

Direct oral anticoagulants (DOACs) should be considered in preference to non-DOAC therapy (a parenteral anticoagulant such as unfractionated heparin (UFH) or low molecular weight heparin (LMWH) overlapped with warfarin) if the patient is an appropriate candidate [1]. Patients must have the following to be a DOAC candidate:

- Adequate renal function: creatinine clearance (CrCl) >30 mL/min (> 25 mL/min for apixaban)
- No significant drug interactions (e.g., carbamazepine, antifungals)
- Confirmed financial coverage for medication
- History of good compliance with medications and/or appointments or highly likely to be adherent
- No allergies or other contraindications

Non-DOAC Therapy for VTE Patients Clinically Unsuitable for DOACs

Clinician to consider non-DOAC therapy (therapeutic dose parenteral anticoagulants or lead-in parenteral with warfarin) for the following indications [1]:

Therapeutic Dose Parenteral Anticoagulants

- ☐ **Cancer-associated venous thromboembolism (CAT):** Both DOACs and LMWH monotherapy may be considered first-line with most cancers [2]
- ☐ **Pregnancy/breastfeeding:** UFH or LMWH (and occasionally warfarin in breastfeeding only) are preferred
- ☐ **Patients with heparin-induced thrombocytopenia (HIT) or a history of HIT:** Consider fondaparinux
- ☐ **Patients with severe renal dysfunction (estimated CrCl <15 ml/min or dialysis):** UFH is preferred over LMWH

Lead-In Parenteral With Warfarin

- ☐ **Antiphospholipid Antibody Syndrome (APAS)**
- ☐ **Severe renal impairment or hemodialysis**
- ☐ **Mechanical valve**
- ☐ **Planned use of dabigatran or edoxaban**

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Factors Influencing Drug Selection

RENAL FUNCTION

Renal and liver characteristics are necessary to determine appropriateness of anticoagulation therapy.

☐ Calculate estimated CrCl using the Cockcroft-Gault formula based on the following:
Age: _____
Actual body weight: _____(kg)
Gender: _____
Serum creatinine: _____ (mg/dL)
Estimated CrCl: _____ (mL/minute)

$$\frac{[(140 - \text{Age}) \times \text{actual weight in kg}]}{[72 \times \text{serum creatinine}]} \quad \text{X 0.85 if female}$$

LIVER FUNCTION

☐ Liver disease: ○ No ○ Yes: Child Pugh Grade: _____

CHILD PUGH SCORE

Measure	1 point	2 points	3 points
Total bilirubin (mg/dL)	< 2	2 - 3	> 3
Serum albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
INR	Less than 1.7	1.7 – 2.2	Greater than 2.2
Ascites	None	Mild (or suppressed with medication)	Moderate to Severe (or refractory)
Hepatic encephalopathy	None	Grade I-II	Grade III-IV

Note: The score employs five clinical measures of liver disease.[3] Each measure is scored 1-3, with 3 indicating the worst condition.

Total Score	Grade	Status
5-6	Grade A	Well-compensated Disease
7-9	Grade B	Significant Functional Compromise
10-15	Grade C	Decompensated Disease

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Factors Influencing Drug Selection Continued…

VTE History (Please Check All That Apply)

- ☐ Provoked VTE (e.g., hormone therapy, surgery within 3 months, leg in a cast, recent immobilization ≥ 3 days)
- ☐ Unprovoked VTE
- ☐ Recurrent proximal DVT or PE
- ☐ VTE present on admission
- ☐ Other (specify):_____

Shared Decision-Making Discussion

Note: If drug costs are a barrier to filling prescriptions for medication, refer patient to appropriate resources.

Select all that have been discussed with patient:

- ☐ Bleeding risk/reversal agents
- ☐ Dosing regimen options (e.g., once vs. twice daily)
- ☐ Lifestyle factors of drug (e.g., diet, blood draws, activities, taken with meals)
- ☐ Out-of-pocket medication cost
- ☐ Other (specify):_____

DOAC Standard Dose

	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Parenteral lead-in (usually LMWH)	None		≥ 5 days, then **SWITCH** to DOAC	
Standard DOAC Dose	10 mg PO BID x 7 days, then 5 mg PO BID	15 mg PO BID x 21 days WITH FOOD, then 20 mg PO daily WITH FOOD	60 mg PO daily	150 mg PO BID

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Factors Influencing Drug Selection Continued….

CONCOMITANT MEDICATION [4]

DOAC DRUG INTERACTIONS AND DOSE ADJUSTMENTS

	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Renal Impairment	Estimated CrCl <25 ml/min: *Avoid use*	Estimated CrCl <30 ml/min: *Avoid use*	Estimated CrCl <30 ml/min: *Avoid use* Estimated CrCl 30-50 ml/min: *30 mg PO daily*	Estimated CrCl ≤30 ml/min: *Avoid use*
Hepatic Impairment	Child-Pugh A: *No adjustment needed* Child-Pugh B: *Avoid or use with caution* Child-Pugh C: *Avoid use*			*No Adjustment*
Body Weight Overweight	Weight >120 kg or BMI over 40: **Appropriate for Use**		Weight >120 kg or BMI over 40: **AVOID USE**	
Low	*No Adjustment*		≤ 60 kg: *30 mg PO daily*	*No Adjustment*
Underweight	Weight <50 kg: *Avoid Use*			
PharmacoDYNAMIC drug interactions	*Avoid or minimize concomitant use of antiplatelets and/or NSAIDs whenever possible*			
PharmacoKINETIC drug interactions	Eliminated/metabolized by: ▪ P-gp efflux transporter system ▪ CYP 3A4 hepatic isoenzyme system		Eliminated by: ▪ P-gp efflux transporter system	
P-gp and/or <u>*strong*</u> 3A4 INDUCERS *(e.g., barbiturates, carbamazepine, dexamethasone, phenytoin, primidone, rifampin, St. John's Wort)**	*Avoid Use*		*No Adjustment*	
P-gp INHIBITORS *(e.g. amiodarone, arvedilol, diltiazem, dronaderone, azithro/clarithro/ erythromycin, oral itra/ketoconazole, quinidine, verapamil)**	*N/A*		*30 mg PO Daily*	Estimated CrCl < 50 ml/min: Avoid Use

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Factors Influencing Drug Selection Continued…

CONCOMITANT MEDICATION [4]

DOAC DRUG INTERACTIONS AND DOSE ADJUSTMENTS CONTINUED…

	Apixaban	*Rivaroxaban*	*Edoxaban*	*Dabigatran*
Dual P-gp and *strong* CYP 3A4 INHIBITORS *(e.g. clarithromycin, oral itra/ ketoconazole, cobicistat, indinavir, ritonavir, saquinivir, teleprevir)**	*Decrease induction and maintenance dose by 50%*	*Avoid Use*	*N/A*	
Dual P-gp and *moderate* CYP 3A4 INHIBITORS *(e.g. cyclosporine, diltiazem, dronaderone, erythromycin, verapamil)**	*Use with Caution*	*Estimated CrCl <80 ml/min: Avoid use*	*N/A*	

**Drug lists are not exhaustive*

Orders

OPTIONS FOR TREATMENT APPROACH [1]

Choose one anticoagulation approach and complete orders as per below:

DOAC Therapy

1. Single Direct Oral Anticoagulant (DOAC) (Rivaroxaban OR Apixaban)
2. Lead-in Parenteral with DOAC (Parenteral PLUS Edoxaban OR Dabigatran)

Non-DOAC Therapy

3. Lead-in Parenteral with Warfarin (Parenteral PLUS Warfarin)
4. Therapeutic Dose Parenteral Only (Dalteparin OR Enoxaparin OR Fondaparinux OR Other)

DOAC THERAPY

1. SINGLE DIRECT ORAL ANTICOAGULANT (DOAC) (RIVAROXABAN OR APIXABAN)

Choose one DOAC and de-escalate dose on _____ *(date)*

APIXABAN

- ☐ Apixaban two 5 mg tablets (10 mg total), PO twice daily for first 7 days, followed by one 5 mg tablet (5 mg total), PO twice daily
- ☐ Apixaban starter pack (single fill for first month of therapy), followed by one tablet (5 mg total), PO twice daily
- ☐ Other (specify): _____

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Orders Continued…

DOAC Therapy Continued….

1. Single Direct Oral Anticoagulant (DOAC) (Rivaroxaban Or Apixaban) Continued…

Rivaroxaban (choose only one)

- ☐ Rivaroxaban 15 mg PO twice daily with food for 21 days, followed by 20 mg PO once daily with food
- ☐ Rivaroxaban starter pack (single fill for first month of therapy) PO daily with food, followed by 20 mg PO once daily with food
- ☐ Other (specify): _____

2. Lead-In Parenteral With DOAC (Parenteral Plus Edoxaban Or Dabigatran)

Choose "A" for requisite 5-day parenteral lead-in, then "B" to switch to DOAC on _____(date)

A. Parenteral Lead-In (choose only one)

Dalteparin

- ☐ 200 IU/kg every 24 hours administered subcutaneously for at least 5 days

Enoxaparin (choose only one)

- ☐ 1 mg/kg every 12 hours administered subcutaneously at the same time every day for at least 5 days
- ☐ 1.5 mg/kg once a day administered subcutaneously at the same time every day for at least 5 days
- ☐ Other (specify):_____

Fondaparinux (choose only one)

- ☐ Fondaparinux 5 mg (body weight <50 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 7.5 mg (50 to 100 kg), subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 10 mg (>100 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Other (specify):_____

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Orders Continued…

DOAC Therapy Continued….

2. Lead-In Parenteral With DOAC (Parenteral Plus Edoxaban Or Dabigatran) Continued….

A. Parenteral Lead-In Continued….

Other Parenteral Anticoagulant

☐ Other (specify):_____

B. DOAC Requiring Parenteral Lead-In (Choose Only One)

Dabigatran

☐ Dabigatran 150 mg PO twice daily *(must leave in original package, take with full glass of water),* preceded by parenteral lead-in indicated below

☐ Other (specify):_____

Edoxaban (choose only one)

☐ Edoxaban 60 mg PO once daily, preceded by parenteral lead-in indicated below
(CrCl greater than ≥ 51 mL/minute)

☐ Edoxaban 30 mg PO once daily, preceded by parenteral lead-in indicated below
(CrCl 30 to 50 mL/minute, with body weight less than or equal to 60 kg, or concomitant P-gp Inhibitor)

☐ Other (specify):_____

Non-DOAC Therapy

3. Lead-In Parenteral With Warfarin (Parenteral PLUS Warfarin)

Choose "A" for requisite 5-day parenteral lead-in and until INR >2, then "B" to switch to Warfarin on _____ (date)

A. Parenteral Lead-In (choose only one)

Dalteparin

☐ 200 IU/kg every 24 hours administered subcutaneously for at least 5 days

Acute VTE Care Transition Order Set (Adult)

ACTION

Orders Continued…

NON-DOAC THERAPY CONTINUED….

3. LEAD-IN PARENTERAL WITH WARFARIN (PARENTERAL PLUS WARFARIN) CONTINUED….

A. Parenteral Lead-In (choose only one) Continued….

Enoxaparin (choose only one)

- ☐ 1 mg/kg every 12 hours administered subcutaneously at the same time every day for at least 5 days
- ☐ 1.5 mg/kg once a day administered subcutaneously at the same time every day for at least 5 days
- ☐ Other (specify):_____

Fondaparinux (choose only one)

- ☐ Fondaparinux 5 mg (body weight <50 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 7.5 mg (50 to 100 kg), subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 10 mg (>100 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Other (specify):_____

Other Parenteral Anticoagulant

- ☐ Other (specify):_____

B. Warfarin Requiring Parenteral Lead-In (choose only one)

- ☐ Warfarin 5 mg PO once daily, then request Physician, NP/PA, Pharmacist, or Anticoagulation Clinic to reassess and adjust
  Consider lower starting doses of warfarin for elderly patients (e.g. >75 yr) and/or those with low body weight (less than or equal to 50 kg)
- ☐ Warfarin 2.5 mg PO once daily, then request Physician, NP/PA, Pharmacist, or Anticoagulation Clinic to reassess and adjust
- ☐ Warfarin _____ PO once daily, then request Physician, NP/PA, Pharmacist, or Anticoagulation Clinic to reassess and adjust
- ☐ Other (specify):_____

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Orders Continued…

NON-DOAC THERAPY CONTINUED….

4. THERAPEUTIC DOSE PARENTERAL ONLY (DALTEPARIN OR ENOXAPARIN OR FONDAPARINUX OR OTHER)

Dalteparin (choose only one)

- ☐ 200 IU/kg every 24 hours administered subcutaneously for 30 days, then 150 IU/kg every 24 hours administered subcutaneously
- ☐ 200 IU/kg every 24 hours administered subcutaneously for at least 5 days

Enoxaparin (choose only one)

- ☐ 1 mg/kg every 12 hours administered subcutaneously at the same time every day for at least 5 days
- ☐ 1.5 mg/kg once a day administered subcutaneously at the same time every day for at least 5 days
- ☐ Other (specify):_____

Fondaparinux (choose only one)

- ☐ Fondaparinux 5 mg (body weight <50 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 7.5 mg (50 to 100 kg), subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Fondaparinux 10 mg (>100 kg) subcutaneously once daily. Treatment should continue for at least 5 days
- ☐ Other (specify):_____

Other Parenteral Anticoagulant

- ☐ Other (specify):_____

BASELINE LAB ORDERS

- ☐ Baseline CBC (for ALL)
- ☐ Baseline INR for warfarin
- ☐ Baseline CMP (for all)
- ☐ Baseline serum creatinine (for ALL)
- ☐ Other (specify):

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Acute VTE Care Transition Order Set (Adult)

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Orders Continued…

FOLLOW-UP LAB ORDERS

DOACS

- ☐ Monitor renal function q3-12 months (e.g., serum creatinine, CrCl)
- ☐ Anticoagulant clinic referral as per policy/procedure [1, 5]
- ☐ Other (specify): _____

NON-DOAC/WARFARIN THERAPY INR

- ☐ Target INR 2 – 3
- ☐ INR q3-4 days for 2 weeks, then as instructed by clinician or Anticoagulation Clinic
- ☐ Anticoagulant Clinic referral as per policy/procedure [1, 5]
- ☐ Other (specify): _____

Other Considerations

ANTIPLATELET THERAPY

Note: Patients who take multiple anti-thrombotic agents (aspirin, NSAIDs, P2Y12 inhibitors [e.g. clopidogrel, prasugrel, ticagrelor] and anticoagulants) are at increased risk for bleeding complications. Clinicians should review the risk-benefit ratio for each medication and consider minimizing bleeding risk whenever possible [6].

- ☐ Patient should **CONTINUE** current ASA therapy
- ☐ Patient should **DISCONTINUE** current ASA therapy
- ☐ Patient should **CONTINUE** current P2Y-12 therapy
- ☐ Patient should **DISCONTINUE** current P2Y-12 therapy
- ☐ Other (specify): _____

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ACTION

Other Considerations Continued…

PROTON PUMP INHIBITORS (PPIS)

Note: Clinician may consider PPI for patients at high risk of GI bleeding, particularly if using multiple antithrombotic agents or with a prior history of upper GI bleeding (7, 8, 9). PPIs may decrease serum concentrations of the active metabolite(s) of dabigatran. PPIs are optimally taken 30 minutes before breakfast.

- ☐ Dexlansoprazole 30 mg PO once daily
- ☐ Esomeprazole 20 mg PO once daily (avoid concomitant use with clopidogrel)
- ☐ Lansoprazole _____ mg PO once daily (15 – 30 mg)
- ☐ Omeprazole 20 mg PO once daily (avoid concomitant use with clopidogrel)
- ☐ Pantoprazole _____ mg PO once daily (20 – 40 mg)
- ☐ Rabeprazole 20 mg PO once daily
- ☐ Other (specify):_____

PATIENT EDUCATION

Provide applicable education and discharge instruction to the patient as per policy/procedure [1, 10].
The following topics are important to include within patient education:

- ☐ Follow-up appointments for blood work
  - ☐ Follow-up contact information:_____
- ☐ Safety net phone number to call if any barriers or issues after discharge: _____
- ☐ Medication management, including starting/stopping new medication, missed doses and dose change (dose de-escalation or switch to oral therapy at appropriate date/time)
- ☐ Importance of medication adherence
- ☐ Expected duration of anticoagulation therapy
- ☐ Appropriate medication storage
- ☐ Drug/diet considerations
- ☐ Bleeding and bruising risks
- ☐ When to seek medical attention (e.g. warning signs for bleeding, symptoms of recurrent VTE)
- ☐ Written education materials for patient/family/caregivers to review after discharge
- ☐ Importance of social support
- ☐ Medication reconciliation completed

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Other Considerations Continued…

REFERRALS

- ☐ Anticoagulation Clinic: _____
- ☐ Hematology: _____
- ☐ Vascular/Cardiovascular Specialist: _____
- ☐ Primary Care Provider: _____
- ☐ Oncology: _____

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Additional Orders

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References

All medications have been reviewed using Lexicomp Online.

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Order Set Updated: October 2022

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