Venous Thromboembolism (VTE) Prophylaxis in Acutely Ill Medical Patients

An AC Forum *Rapid Resource*

Presenters:

Allison Burnett, PharmD | Steve Deitelzweig, MD, MMM

Scott Kaatz, DO, MSc | Ronni Nemeth, PharmD, CACP, DPLA

Presenters

Allison Burnett, PharmD, CACP, PhC

- Lead Inpatient Antithrombosis Stewardship Pharmacist, University of New Mexico Hospital
- Associate Clinical Professor, University of New Mexico, College of Pharmacy

Scott Kaatz, DO, MSc, SFHM

- Clinical Professor of Medicine, Wayne State University School of Medicine
- Senior Staff Hospitalist, Medical Director for Professional Development and Research, Division of Hospital Medicine, Henry Ford Hospital

Steve Deitelzweig, MD, MMM

- System Chairman for Hospital Medicine and Medical Director of Regional Business Development, Ochsner Health System
- Professor of Medicine, Ochsner Health System/University of Queensland

Ronni Nemeth, PharmD, CACP, DPLA

- Manager, Anticoagulation Clinics, Confluence Health
- Co-chair of Confluence Health Anticoagulation Steering Committee

Disclosures & Notification of Support

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The below speaker disclosure has the listed relevant financial relationships with commercial interests:

Scott Kaatz, DO, MSc

Bristol-Myers Squibb (BMS) | Osmosis | Janssen Pharmaceuticals | Pfizer Pharmaceuticals Inc | Novartis | Portola/Alexion Pharmaceuticals | Gilead Sciences

Steve Deitelzweig, MD, MMM

Portola/Alexion Pharmaceuticals | Bristol-Myers Squibb (BMS) | Pfizer Pharmaceuticals Inc

Background and Scope

- In 2008 the surgeon general issued a Call to Action to prevent DVT and PE and recognized VTE as a significant public health concern.[1]

- In 2020, the American Heart Association issued a Call to Action for better implementation of VTE risk stratification, prevention, and tracking.[2]

- Up to 70-80% of VTE events occur after hospital discharge with length of stay being much shorter now than in seminal studies that used 6-14 days of LMWH.[3]

Office of the Surgeon General (US); 2008. PMID: 20669525
Henke PK. Circulation. 2020. PMID: 32375490
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VTE in Medically Ill Patients

- Half of VTE events occur due to hospital admission for surgery (24%) or medical illness (22%)
- Risk factors for VTE in hospital include cancer, advanced age, prior VTE, central lines, immobility
- 40% of hospitalized patients have 3 or more risk factors for VTE
- Increase in thrombosis risk in medical inpatients persists 45-60 days after discharge

Blood Advances 2018. PMID: 30482763

CY 2021 VTE-1 and VTE-2 eCQMs

Assesses the number of hospitalized adult patients who received VTE prophylaxis (pharmacological or mechanical prophylaxis), or have documentation why no VTE prophylaxis was given for:

- VTE-1: The day of or the day after (1) hospital admission; or (2) the surgery end date for surgeries that start the day of or the day after hospital admission
- VTE-2: The day of or the day after (1) the initial admission (or transfer) to the ICU; or (2) surgery end date for surgeries that start the day of or the day after ICU admission or transfer

Updates: CMS updated VTE-1 and 2 logic to include rivaroxaban as approved medication administration for VTE prophylaxis in medically ill patients as it has FDA approval

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BOTTOM LINE

DO	DON'T	CONSIDER	CAUTION
• Use VTE risk assessment at admission, throughout hospitalization, and at discharge[3] • Use bleeding risk assessment[3] • Use pharmacologic prophylaxis in patients with high VTE risk and acceptable bleeding risk[3] • Use mechanical prophylaxis in patients with high VTE risk and high bleeding risk[3] • Use low molecular weight heparin (LMWH) instead of unfractionated heparin (UFH) in patients with adequate renal function[3]	• Do not give all patients VTE prophylaxis indiscriminately without risk assessment • Do not use combined pharmacologic and mechanical prophylaxis in medically ill patients[3]	• Extended post-discharge VTE prophylaxis in appropriate patients (see criteria below)[3]	• This information is based on expert opinion in the absence of robust data • Some patients will be appropriate for a different approach

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Scope:
Hospitalized non-surgical medically and critically ill patients
Considerations for extended duration thromboprophylaxis (EDT) among high risk medically ill patients at discharge

Pharmacologic Dosing Options

Enoxaparin

Standard Dosing	40mg SC once daily
CrCl <30mL/min	30mg SC once daily
CrCl <20mL/min	Avoid use
Obese patients (BMI > 40kg/m²)	40 mg BID 60mg BID (BMI >47kg/m²)[6,12] 0.5mg/kg QD[9]

Dalteparin

Standard Dosing	5000 units SC once daily
CrCl <30mL/min	Avoid use
Obese patients (BMI > 40kg/m²)	7500 units SC once daily[10,11]

Unfractionated Heparin (UFH)

Standard Dosing	5000 units SC 8-12 hours
Obese patients (BMI>40kg/m2)	7500 units BID-TID*[9,10] *Evidence is limited.

Fondaparinux

Standard Dosing (pt wt ≥50kg)	2.5mg SC once daily
Wt <50 kg or CrCL< 30 mL/min	Avoid use

Rivaroxaban*

Standard Dosing (Extended Duration)	10mg once daily continued for 31-39 days total

*Indicated for use during hospitalization and post-hospital discharge in adults admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE and not at high risk of bleeding (refer to criteria chart)

Cockcroft-Gault should be used to calculate CrCl

Examples of Risk Assessment Models[4]

Several VTE risk assessment models (RAMs) exist, none of which have been extensively studied in impact analysis. As such, contemporary guidelines do not give preference to any single RAM. Rather, it is suggested to use a validated RAM to assess both VTE risk and bleeding risk to identify patients who are (and who are not) at sufficient risk for prophylaxis and preferred treatment modality (pharmacologic vs mechanical)[3].

Padua VTE: Low risk: 0-3 High risk: ≥4		IMPROVE VTE 7: Low risk: 0-1 High risk: ≥2		IMPROVE VTE 4: Low risk: 0-1 High risk: ≥2		*IMPROVE Bleeding*: Low risk: <7 High risk: ≥7	
Risk Factor	Score	Risk Factor	Score	Risk Factor	Score	Risk Factor	Score
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Active cancer	3	Known thrombophilia	2	Malignancy (treated or untreated w/in 6 months)	1	Current cancer	2
Previous VTE	3	Lower limb paralysis	2	Thrombophilia	3	Rheumatic disease	2
Known thrombophilic condition	3	Active cancer	2	Age >60 yrs	1	Central venous catheter	2
Recent trauma and/or surgery (<1mo)	2	Immobilization ≥7d	1			ICU/CCU stay	2.5
Elderly age (>70yr)	1	ICU/CCU stay	1			Hepatic failure (INR>1.5)	2.5
Heart and/or respiratory failure	1	Age >60yr	1			GFR <30 mL/min/m²	2.5
Acute MI or ischemic stroke	1					GFR 30-59 mL/min/m²	1
Ongoing hormonal tx	1					Age 40-84 yr	1.5
Obesity (BMI>30)	1					Age ≥ 85yr	3.5
Acute infection and/or rheumatologic disorder	1					Gastroduodenal ulcer	4.5
						Bleeding in prior 3 months	4
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Low Risk: Do not require prophylaxis[4]
High Risk: Should receive in-hospital prophylaxis[4]
High Bleeding Risk: Might indicate preference for mechanical prophylaxis while bleeding is high; reassessment is warranted[4]

Extended Duration Thromboprophylaxis (EDT)[5]

Rationale: Up to 70-80% of VTE occur after hospital discharge.
Length of stay is now much shorter than in seminal studies that utilized 6-14 days of LMWH[7]

The following criteria pertain to rivaroxaban, which is currently the only commercially available, FDA-approved agent for EDT.

Consider rivaroxaban 10 mg PO daily for a total of up to 39 days in patients who meet selection criteria below:

For patients aged >60 and hospitalized for ≥1 of the following acute medical conditions:
Decompensated heart failure • Respiratory insufficiency or COPD exacerbation • Infectious or inflammatory disease
Ischemic stroke with lower extremity paresis and reduced mobility

OR

For patients aged 40-59, hospitalized for ≥ 1 of the above acute medical illnesses AND
Have history of prior VTE or active cancer AND ≥1 of the below additional VTE risk factor(s):
Previous VTE or superficial vein thrombosis • History of NYHA Class III or IV HF • Concomitant acute infection
Obesity (BMI >35) • History of cancer • Inherited or acquired thrombophilia
Current use of erythropoiesis-stimulating agent • Hormone therapy

Exclusion Criteria:
Contraindications to anticoagulant prophylaxis • Creatinine Clearance <30mL/min
Concomitant combined P-gp and strong CYP3A4 inhibitors and inducers • Pregnant or breastfeeding
Currently on dual antiplatelet therapy (DAPT) • Active bleeding within the last 3 months
Gastroduodenal ulcers within the last 3 months
History of bronchiectasis, pulmonary cavitation, or pulmonary hemorrhage
Active cancer (undergoing acute in-hospital cancer treatment)

Bolded exclusion criteria have been linked to increased fatal or major bleeding events[5]

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• Use bleeding risk assessment[3]	• Do not use combined pharmacologic and mechanical prophylaxis in medically ill patients[3]		• Some patients will be appropriate for a different approach
• Use pharmacologic prophylaxis in patients with high VTE risk and acceptable bleeding risk[3]			
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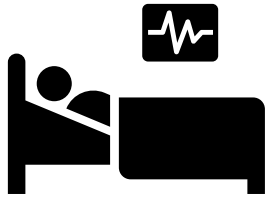
Case Part 1

65-year-old admitted to the medical ward for CHF exacerbation
No history of VTE, cancer or thrombophilia
Normal renal and liver function
No increased bleeding risk
Normal weight
COVID-19 negative

Would you prescribe VTE prophylaxis?

a) Yes
b) No



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Acute Myocardial ischemic stroke	1					GFR 30-59 mL/min/m²	1
Ongoing hormonal Rx	1					Age 40-84 yr	1.5
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Case Part 1

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No history of VTE, cancer or thrombophilia
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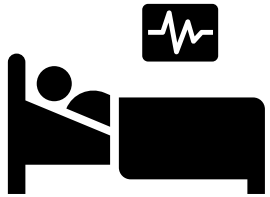
What would you do for VTE prophylaxis?

a) Heparin 5000 units SQ tid
b) Enoxaparin 40 mg SQ daily
c) Pneumatic compression devices
d) No prophylaxis needed



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Gastroduodenal ulcers within the last 3 months
History of bronchiectasis, pulmonary cavitation, or pulmonary hemorrhage
Active cancer (undergoing acute in-hospital cancer treatment)

Bolded exclusion criteria have been linked to increased fatal or major bleeding events[5]

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Support for this project provided by Janssen Pharmaceuticals, Inc.

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Pharmacologic Dosing Options

Enoxaparin

Standard Dosing	40mg SC once daily
CrCl <30mL/min	30mg SC once daily
CrCl <20mL/min	Avoid use
Obese patients (BMI > 40kg/m^2)	40 mg BID 60mg BID (BMI >47kg/m^2)[6,12] 0.5mg/kg QD[8]

Dalteparin

Standard Dosing	5000 units SC once daily
CrCl <30mL/min	Avoid use
Obese patients (BMI > 40kg/m^2)	7500 units SC once daily[10,11]

Unfractionated Heparin (UFH)

Standard Dosing	5000 units SC 8-12 hours
Obese patients (BMI>40kg/m2)	7500 units BID-TID* [9,10] *Evidence is limited.

Fondaparinux

Standard Dosing (pt wt ≥50kg)	2.5mg SC once daily
Wt <50 kg or CrCL< 30 mL/min	Avoid use

Rivaroxaban*

Standard Dosing (Extended Duration)	10mg once daily continued for 31-39 days total

*Indicated for use during hospitalization and post-hospital discharge in adults admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE and not at high risk of bleeding (refer to criteria chart)

Cockcroft-Gault should be used to calculate CrCl

Case Part 2

After 3 days in the hospital, the patient develops pneumonia, sepsis and requires intubation and mechanical ventilation.

Would you prescribe VTE prophylaxis?

a) Yes
b) No

What would you do for VTE prophylaxis?

a) Heparin 5000 units tid
b) Enoxaparin 40 mg daily
c) Pneumatic compression
d) No prophylaxis needed

They are extubated and discharged from ICU 5 days later back to the floor. Kidney and liver function are normal

Would you prescribe VTE prophylaxis?

a) Yes
b) No

What would you do for VTE prophylaxis?

a) Heparin 5000 units tid
b) Enoxaparin 40 mg daily
c) Pneumatic compression
d) No prophylaxis needed

Case 3

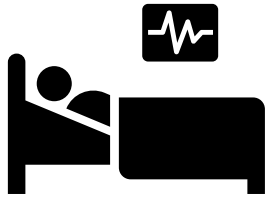
3 days after returning to the floor the patient is ready for discharge, CHF and pneumonia are improved.

Patient is weak but does not require physical therapy.

Would you prescribe extended-duration prophylaxis EDT?

a) Yes

b) No



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Rapid Resource

Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence

Venous Thromboembolism (VTE) Prophylaxis in Acutely Ill Medical Patients

excellence.acforum.org

BOTTOM LINE

DO	DON'T	CONSIDER	CAUTION
• Use VTE risk assessment at admission, throughout hospitalization, and at discharge[3] • Use bleeding risk assessment[3] • Use pharmacologic prophylaxis in patients with high VTE risk and acceptable bleeding risk[3] • Use mechanical prophylaxis in patients with high VTE risk and high bleeding risk[3] • Use low molecular weight heparin (LMWH) instead of unfractionated heparin (UFH) in patients with adequate renal function[3]	• Do not give all patients VTE prophylaxis indiscriminately without risk assessment • Do not use combined pharmacologic and mechanical prophylaxis in medically ill patients[3]	• Extended post-discharge VTE prophylaxis in appropriate patients (see criteria below)[3]	• This information is based on expert opinion in the absence of robust data • Some patients will be appropriate for a different approach

Background:
In 2008 the surgeon general issued a Call to Action to prevent DVT and PE and recognized VTE as a significant public health concern.[1]

In 2020, the American Heart Association issued a call to action for better implementation of VTE risk stratification, prevention and tracking.[2]

Scope:
Hospitalized non-surgical medically and critically ill patients

Considerations for extended duration thromboprophylaxis (EDT) among high risk medically ill patients at discharge

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Cockcroft-Gault should be used to calculate CrCl

Examples of Risk Assessment Models[4]

Several VTE risk assessment models (RAMs) exist, none of which have been extensively studied in impact analysis. As such, contemporary guidelines do not give preference to any single RAM. Rather, it is suggested to use a validated RAM to assess both VTE risk and bleeding risk to identify patients who are (and who are not) at sufficient risk for prophylaxis and preferred treatment modality (pharmacologic vs mechanical)[3].

Padua VTE: Low risk: 0-3 High risk: ≥4		IMPROVE VTE 7: Low risk: 0-1 High risk: ≥2		IMPROVE VTE 4: Low risk: 0-1 High risk: ≥2		*IMPROVE Bleeding*: Low risk: <7 High risk: ≥7	
Risk Factor	**Score**	**Risk Factor**	**Score**	**Risk Factor**	**Score**	**Risk Factor**	**Score**
Reduced mobility	3	Previous VTE	3	Previous VTE	3	Male	1
Active cancer	3	Known thrombophilia	2	Malignancy (treated or untreated w/in 6 months)	1	Current cancer	2
Previous VTE	3	Lower limb paralysis	2	Thrombophilia	3	Rheumatic disease	2
Known thrombophilic condition	3	Active cancer	2	Age >60 yrs	1	Central venous catheter	2
Recent trauma and/or surgery (<1mo)	2	Immobilization ≥7d	1			ICU/CCU stay	2.5
Elderly age (>70yr)	1	ICU/CCU stay	1			Hepatic failure (INR>1.5)	2.5
Heart and/or respiratory failure	1	Age >60yr	1			GFR <30 mL/min/m²	2.5
Acute MI or ischemic stroke	1					GFR 30-59 mL/min/m²	1
Ongoing hormonal tx	1					Age 40-84 yr	1.5
Obesity (BMI>30)	1					Age ≥ 85yr	3.5
Acute infection and/or rheumatologic disorder	1					Gastroduodenal ulcer	4.5
						Bleeding in prior 3 months	4
						Admission platelets <50,000	4

Low Risk: Do not require prophylaxis[4]
High Risk: Should receive [illegible] prophylaxis[4]
High Bleeding Risk: [illegible] indicate preference for mechanical prophylaxis [illegible] bleeding is high; reassessment is warranted[4]

Extended Duration Thromboprophylaxis (EDT)[5]

Rationale: Up to 70-80% of VTE occur after hospital discharge.
Length of stay is now much shorter than in seminal studies that utilized 6-14 days of LMWH[7]

The following criteria pertain to rivaroxaban, which is currently the only commercially available, FDA-approved agent for EDT.

Consider rivaroxaban 10 mg PO daily for a total of up to 39 days in patients who meet selection criteria below:

For patients aged >60 and hospitalized for ≥1 of the following acute medical conditions:
Decompensated heart failure • Respiratory insufficiency or COPD exacerbation • Infectious or inflammatory disease
Ischemic stroke with lower extremity paresis and reduced mobility

OR

For patients aged 40-59, hospitalized for ≥ 1 of the above acute medical illnesses AND
Have history of prior VTE or active cancer AND ≥1 of the below additional VTE risk factor(s):
Previous VTE or superficial vein thrombosis • History of NYHA Class III or IV HF • Concomitant acute infection
Obesity (BMI >35) • History of cancer • Inherited or acquired thrombophilia
Current use of erythropoiesis-stimulating agent • Hormone therapy

Exclusion Criteria:
Contraindications to anticoagulant prophylaxis • Creatinine Clearance <30mL/min
Concomitant combined P-gp and strong CYP3A4 inhibitors and inducers • Pregnant or breastfeeding
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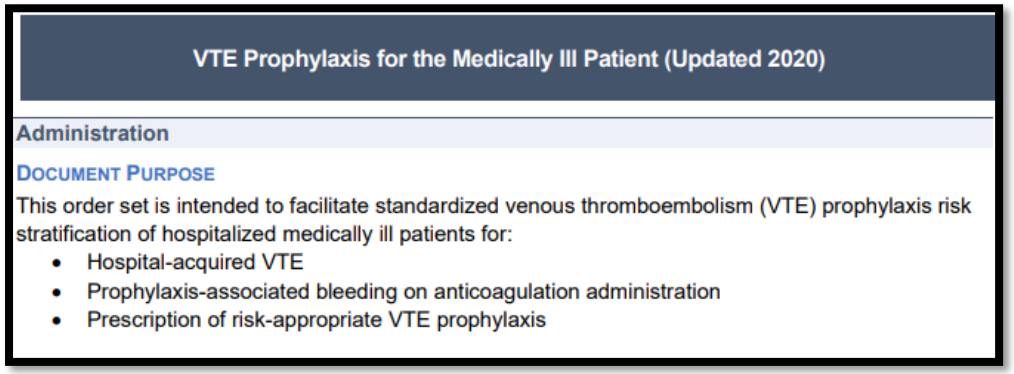
Anticoagulation Stewardship Considerations

- Confirmation of access to medication (e.g., insurance coverage)
- Clear documentation of a finite duration of therapy
- Education and empowerment of patient/family on appropriate use

AC Forum Resource-Order Set

Anticoagulation Forum - VTE prophylaxis for the medically ill patient Order Set, March 2020

Updated by AC Forum 3/2020, this order set is intended to facilitate standardized venous thromboembolism (VTE) prophylaxis risk stratification of hospitalized medically ill patients for: Hospital-acquired VTE, prophylaxis-associated bleeding on anticoagulation administration and prescription of risk-appropriate VTE prophylaxis



VTE Prophylaxis for the Medically Ill Patient (Updated 2020)

Administration

DOCUMENT PURPOSE

This order set is intended to facilitate standardized venous thromboembolism (VTE) prophylaxis risk stratification of hospitalized medically ill patients for:

- Hospital-acquired VTE
- Prophylaxis-associated bleeding on anticoagulation administration
- Prescription of risk-appropriate VTE prophylaxis

Anticoagulation FORUM | Webinar

Support for this project was provided by Janssen Pharmaceuticals, Inc.

The content was developed independently by the Anticoagulation Forum and the funder had no input in the content of the Rapid Resource or webinar