Venous Thromboembolism Prophylaxis

The following chart provides information to guide decisions regarding VTE prophylaxis in common clinical scenarios. See our chart, *LMWH Dosing in Special Populations*, for dosing in under- or overweight patients, patients with kidney impairment, and pregnant/lactating patients. Our chart, *Anticoagulants in Pregnancy*, has additional information pertinent to this population.

Clinical Scenario	VTE Prophylaxis Options
NONsurgical INPATIENT with HIGH VTE RISK. Per ACCP guidelines, medical patients at **high risk of VTE** are those with a ≥4 Padua Prediction Score (see https://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/vtguide/appendixb2.html#b12). The IMPROVE VTE and bleeding risk scores might also be used to guide decision-making (https://www.outcomes-umassmed.org/IMPROVE/). Net benefit of prophylaxis continued beyond hospitalization is unlikely (e.g., for rivaroxaban continued for 45 days post-discharge, NNT = 417 to prevent one symptomatic VTE; NNH = 175 to cause clinically important bleeding).[17]	
High VTE risk, bleeding, or at high risk of bleeding	• Graduated compression stockings, or IPC for at least 18 hrs per day, for duration of immobilization or acute admission.[1]

High VTE risk, not bleeding, and not at high risk of bleeding	• Continue one of the following **for the duration of inpatient immobilization or acute admission**[1,20] (see exception for rivaroxaban, below).
	  • **LMWH**
	  • enoxaparin 40 mg SQ once daily (30 mg SQ once daily if CrCl <30 mL/min [Canada: 20 or 30 mg])[2,3]
	  • dalteparin 5,000 units SQ once daily.[6,7] Consider dose reduction (Canada) or monitoring factor Xa levels (US) in patients with severe kidney impairment (CrCl <30 mL/min).[6,7]
	  • nadroparin (Canada): 3,800 units (if ≤70 kg) to 5,700 units (>70 kg) SQ once daily.[8] Reduce dose by 25% to 33% if CrCl <30 mL/min. Also consider dose reduction for CrCl <50 mL/min.[8]
	  • **fondaparinux** (non-critical care patients[1,20]): 2.5 mg SQ once daily (avoid if CrCl <30 mL/min [contraindicated per US labeling]).[4,5,18]
	  • **heparin** 5,000 units SQ every eight to 12 hrs or 7,500 units SQ every 12 hrs.[10] (ASH: not preferred.[20])
	• Extended thromboprophylaxis with **rivaroxaban** (*Xarelto* for 31 to 39 days) per US labeling.[21] Not proven more effective than standard-duration enoxaparin.[21] (Note: new; not included in ACCP guidelines; ASH recommends inpatient-only LMWH instead.[20]) See our chart, *Comparison of Oral Anticoagulants*, for dosing, drug interactions, and therapeutic considerations.

Clinical Scenario	VTE Prophylaxis Options
SURGICAL patient, NON-hip/knee arthroplasty. To assess VTE risk, the Caprini score (available at: https://capriniriskscore.org/assessment/) can be used.[12] For information on VTE prophylaxis post-hip/knee arthroplasty, see our chart, *VTE Prevention After Hip or Knee Replacement*.	
For **general or abdominal/pelvic surgery** patients at **low** risk of VTE (e.g., Caprini score 1 to 2)	• Mechanical prophylaxis (preferably with IPC for at least 18 hrs per day) is suggested.[12] • Optimal duration unknown. Continue at least until discharge.[14]
For **general or abdominal/pelvic surgery** patients at **moderate** risk of VTE (e.g., Caprini score 3 to 4), major bleeding **not** a concern	**Suggested options**: • LMWH (see footnote a)[12] OR • heparin 5,000 units SQ every eight to 12 hrs[12] OR • mechanical prophylaxis, preferably with IPC for at least 18 hrs per day.[12] • Optimal duration unknown. Continue at least until discharge.[14]
For **general or abdominal/pelvic surgery** patients at **moderate** risk of VTE (e.g., Caprini score 3 to 4), major bleeding a concern	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day is suggested.[12] • Optimal duration unknown. Continue at least until discharge.[14]
For **general or abdominal/pelvic surgery** patients at **high** risk of VTE (e.g., Caprini score ≥5), major bleeding **not** a concern	**Recommended options**: • LMWH (see footnote a)*[12] OR • heparin 5,000 units SQ every eight to 12 hrs*[12] AND • It is also suggested that elastic compression stockings, or IPC for at least 18 hrs per day, be **added**.[12] *If major bleeding is **not** a concern, but the patient cannot receive LMWH or heparin (e.g., allergy), alternative may include low-dose aspirin, fondaparinux (see footnote a), or mechanical prophylaxis, preferably IPC for at least 18 hrs per day.[12] • For patients undergoing abdominal or pelvic surgery **for cancer**, it is recommended that LMWH be continued for four weeks.[12] **For others**, optimal duration unknown. Continue at least until discharge.[14]

Clinical Scenario	VTE Prophylaxis Options
SURGICAL patient, NON-hip/knee arthroplasty, continued	
For **general or abdominal/pelvic surgery** patients at **high** risk of VTE (e.g., Caprini score ≥5), major bleeding a concern	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is recommended.[12] • Optimal duration unknown. Continue until discharge.[14]
Cardiac surgery, uncomplicated post-op course	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is recommended.[12] • Optimal duration unknown. Continue until discharge.[14]
Cardiac surgery, post-op course prolonged due to **nonhemorrhagic** surgical complication	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is recommended.[12] AND • Addition of LMWH (see footnote a) or heparin 5,000 units SQ every eight to 12 hrs is suggested.[12] • Optimal duration unknown. Continue until discharge.[14]
Thoracic surgery, **moderate** VTE risk, not at high bleeding risk	**Suggested options**: • LMWH (see footnote a)[12] OR • heparin 5,000 units SQ every eight to 12 hrs[12] OR • mechanical prophylaxis, preferably with IPC for at least 18 hrs per day.[12] • Optimal duration unknown. Continue at least until discharge.[14]
Thoracic surgery, **high** VTE risk, not at high bleeding risk	**Suggested options**: • LMWH (see footnote a)[12] OR • heparin 5,000 units SQ every eight to 12 hrs*[12] AND • It is also suggested that elastic compression stockings, or IPC for at least be 18 hrs per day, be **added**.[12] • Optimal duration unknown. Continue at least until discharge.[14]
Thoracic surgery, **moderate** VTE risk, high **bleeding risk**	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is suggested.[12] • Optimal duration unknown. Continue at least until discharge.[14]

Clinical Scenario	VTE Prophylaxis Options
SURGICAL patient, NON-hip/knee arthroplasty, continued	
Craniotomy, not at very high VTE risk	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is suggested.[12] • Optimal duration unknown. Continue until discharge.[14]
Craniotomy, **very high** VTE risk (e.g., cancer surgery)	• It is suggested that pharmacologic prophylaxis can be added to mechanical prophylaxis once hemostasis has been achieved and risk of bleeding has decreased (e.g., at least 12 to 24 hrs post-op).[12] • Optimal duration unknown. Continue at least until discharge.[14]
Spinal surgery, not at very high VTE risk	• Mechanical prophylaxis, preferably with IPC for at least 18 hrs per day, is suggested.[12] • Optimal duration unknown. Continue until discharge.[14]
Spinal surgery, **very high** VTE risk (e.g., cancer, combined anterior-posterior approach)	• It is suggested that pharmacologic prophylaxis can be added to mechanical prophylaxis once hemostasis has been achieved and risk of bleeding has decreased.[12] • Optimal duration unknown. Continue at least until discharge.[14]
Surgical patient, HIP/KNEE ARTHROPLASTY. For information on VTE prophylaxis post-hip/knee arthroplasty, see out chart, *VTE Prevention After Hip or Knee Replacement.*	
TRAUMA INPATIENTS	
Not at high VTE risk	**Suggested options**: • LMWH (see footnote a)[12] OR • heparin 5,000 units SQ every eight to 12 hrs[12] OR • mechanical prophylaxis, preferably with IPC for at least 18 hrs per day.[12] • Optimal duration unknown. Consider continuing until discharge from rehab.[14]
With high VTE risk (e.g., acute spinal cord injury, surgery for spinal injury, traumatic brain injury).	• It is suggested that pharmacology and mechanical prophylaxis (as above) be combined, if not contraindicated by lower extremity injury.[12] • Optimal duration unknown. Continue until discharge from rehab.[14] For spinal cord injury, it is reasonable to continue prophylaxis for three months, but a shorter course may be appropriate for patients who regain purposeful lower extremity movement.[12]

Clinical Scenario	VTE Prophylaxis Options
CANCER (outpatients)	
No additional VTE risk factors	• It is suggested that prophylaxis (i.e., LMWH, heparin) **not** be routinely used. If prophylaxis is used, warfarin use is not recommended.[1]
With solid tumor and additional risk factor (history of VTE; immobilization; or treatment with hormone therapy, angiogenesis inhibitor, thalidomide, or lenalidomide)[1]	**Suggested options** (Canada: LMWH preferred):[1,13] • enoxaparin 40 mg SQ once daily.[11] Per labeled dosing for medical patients, 30 mg SQ once daily if CrCl <30 mL/min (Canada: 20 or 30 mg).[2,3] OR • dalteparin 5,000 units SQ once daily.[13] Per labeling for medical patients, consider dose reduction (Canada) or monitoring factor Xa levels (US) in patients with severe kidney impairment (CrCl <30 mL/min).[6,7] OR • tinzaparin (Canada) 4,500 units or 75 units/kg SQ once daily.[11,13] Per labeled dosing for surgical patients, use caution and consider dose reduction if CrCl <30 mL/min.[9] OR • nadroparin (Canada): 35 to 75 units/kg SQ once daily.[11] Per labeled dosing for medical patients 3,800 units (if ≤70 kg) to 5,700 units (>70 kg) SQ once daily.[8] Reduce dose by 25% to 33% if CrCl <30 mL/min., and also consider reducing dose for CrCl <50 mL/min.[8] OR • heparin 5,000 units SQ every eight to 12 hrs or 7,500 units SQ every 12 hrs.[10]
HISTORY of VTE, long-term prophylaxis after treatment (i.e., extended duration)	
VTE **provoked** by a **transient** risk factor, no active cancer or persistent risk factor (e.g., antiphospholipid syndrome)	• In the setting of a **MAJOR transient risk factor** (e.g., surgery with general anesthesia for >30 min., confinement to hospital bed for ≥3 days, cesarean section, major trauma) within the three months prior to the VTE, offering extended prophylaxis is recommended **against**.[15] • In the setting of a **MINOR transient risk factor** (e.g., surgery with general anesthesia for <30 min., hospital admission <3 days, outpatient bed rest or leg injury with reduced mobility for ≥3 days, prolonged plane or car travel, estrogen use, pregnancy or post-partum) within the two months prior to the VTE, offering extended prophylaxis is suggested **against**.[15]
VTE (first or recurrent), **unprovoked** or **provoked** by a **persistent** risk factor (e.g., **active cancer** [also see below], antiphospholipid syndrome)	• Offering extended prophylaxis with a DOAC (e.g., rivaroxaban 10 mg once daily, apixaban 2.5 mg twice daily) is **recommended**.[15] Consider risk/benefit and patient preference.[15] o Use warfarin if a DOAC can't be used.[15] Aspirin could be used but is much less effective than anticoagulants, with similar bleeding risk.[15] • See our chart, *Comparison of Oral Anticoagulants*, for dosing, drug interactions, and more. • Assess decision to continue use at least yearly and when clinical circumstances change.[15]

Clinical Scenario	VTE Prophylaxis Options
HISTORY of VTE, long-term prophylaxis after treatment (i.e., extended duration), continued	
VTE, **active cancer**	• See our chart, *Cancer-Associated Thrombosis FAQs*, for additional guidance.[15]
Long-Distance TRAVELERS (e.g., trip lasting >4 hrs[22])	
Long distance travelers not otherwise at increased risk of VTE	• Graduated compression stockings, aspirin, and anticoagulants are NOT routinely recommended.[1,16,20] • General preventive measures are recommended.[16] For example: o walking every two or three hrs.[22] o choosing an aisle seat (lower VTE risk than window seat).[16] o exercises (e.g., ankle rolls or raises, leg stretches).[16,22,23] o not crossing legs.[24] o hydration and avoidance of alcohol and caffeine (dehydration is a risk factor).[16,19]
High VTE risk (e.g., recent surgery or trauma, VTE history, active cancer, pregnancy, estrogen replacement, oral contraceptives use, elderly, severe obesity, thrombophilic disorder)[1,16,19]	• **ACCP**: Frequent ambulation, aisle seating, and calf exercises are suggested. Below-knee graduated compression stockings with 15 to 30 mm Hg at the ankle are also suggested.[1] Guidelines suggest **against** aspirin or anticoagulants specifically for this use.[1] • **ACOG**: During pregnancy, support stockings, exercise/ambulation, loose clothing, and hydration can be advised.[25] • **Thrombosis Canada**: For patients with previous unprovoked or travel-related VTE, active cancer, recent surgery or trauma, ≥2 risk factors, including combinations of the above with obesity, limited mobility, advanced age, known thrombophilia, pregnancy, or estrogen use: if not on anticoagulation, graduated compression stockings at a strength of 20 to 30 mm Hg are recommended. In patients at very high-risk of thrombosis not already on an anticoagulant, a short course of anticoagulation (i.e., a single dose of LMWH [e.g., enoxaparin 1 mg/kg] or DOAC [less evidence] two to four hrs pre-flight[19]) could be considered (weighing risks and benefit and considering patient values and preferences).[16,19] • **ASH**: For patients with recent surgery, VTE history, postpartum, active cancer, or ≥2 risk factors, including combinations of the above with estrogen replacement, obesity, or pregnancy: graduated compression stockings or prophylactic LMWH (e.g., enoxaparin 1 mg/kg two to four hrs pre-flight[19]) is suggested for travel >4 hrs. If neither is feasible, aspirin is suggested.[20]

Clinical Scenario	VTE Prophylaxis Options
Other OUTPATIENT Scenarios	
Extended-duration VTE prophylaxis in non-surgical medical patients	• Inpatient-only prophylaxis recommended over extended-duration prophylaxis in non-surgical medical patients.[20] ○ Prophylaxis continued beyond hospitalization has not proven net benefit vs in-hospital prophylaxis only.[17]
Outpatients with minor VTE risk factors (e.g., immobility, minor injury, infection, illness)	• VTE prophylaxis not recommended.[20]
Chronically immobilized patient at home or in a care facility	• It is suggested that prophylaxis not be routinely used.[1,20]
Thrombophilia, no VTE history	• VTE prophylaxis not recommended.[1]

Abbreviations: ACOG = American College of Obstetrics and Gynecology; ASH = American Society of Hematology; ACCP = American College of Chest Physicians; CrCl = creatinine clearance; DOAC = direct-acting oral anticoagulant; DVT = deep vein thrombosis; hrs = hours; IPC = intermittent pneumatic compression; LMWH = low-molecular-weight heparin; SQ = subcutaneous; VTE = venous thromboembolism.

a. **LMWH** and **fondaparinux** dosing for **surgical** patients (note: ACCP guidelines recommend consulting labeling for dosing. FDA and Health Canada labeling is based on data in abdominal or general surgery).[12]
   - **enoxaparin** (abdominal surgery): 40 mg SQ once daily, started two hrs pre-op (30 mg SQ once daily if CrCl <30 mL/min [Canada: 20 or 30 mg]), usually for seven to ten days (Canada: up to four weeks).[2,3]
   - **dalteparin** (abdominal surgery [US], general surgery [Canada]): 2,500 units SQ once daily starting one to two hrs pre-op. If high-risk (e.g., cancer) 5,000 units SQ once daily starting the evening before surgery **or** 2,500 units SQ one to two hrs pre-op, then 2,500 units 12 hrs later (Canada: no sooner than four hrs post-op and at least eight hrs after the previous dose, once hemostasis achieved), then 5,000 units once daily. Usually continued for five to ten days (Canada: at least five to seven days).[6,7] Consider dose reduction (Canada) or monitoring factor Xa levels (US) in patients with severe kidney impairment (CrCl <30 mL/min).[6,7]
   - **nadroparin** (Canada; general surgery): 2,850 units SQ once daily starting two to four hrs pre-op. Continue for at least seven days.[8] Reduce dose by 25% to 33% if CrCl <30 mL/min., and also consider for CrCl <50 mL/min.[8]
   - **tinzaparin** (Canada; general surgery): 3,500 units SQ once daily for seven to ten days, starting two hrs pre-op. Use caution and consider dose reduction if CrCl <30 mL/min.[9]
   - **fondaparinux** (abdominal surgery): 2.5 mg SQ once daily, usually for five to nine days (up to ten days in clinical trials), starting no sooner than six to eight hrs post-op, once hemostasis achieved; not for patients with severe kidney impairment.[4,5,18]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

References

1. Kahn SR, Lim W, Dunn AS, et al. Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e195S-e226S.
2. Product information for Lovenox. Sanofi-Aventis US. Bridgewater, NJ 08807. December 2021.
3. Product monograph for Lovenox. Sanofi-Aventis Canada. Laval, QC H7V 0A3. September 2021.
4. Dentali F, Douketis JD, Gianni M, et al. Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. Ann Intern Med. 2007 Feb 20;146(4):278-88.
5. Product information for Arixtra. Mylan Institutional. Morgantown, WV 26505. August 2020.
6. Product information for Fragmin. Pfizer Labs. New York, NY 10017. June 2020.
7. Product monograph for Fragmin. Pfizer Canada. Kirkland, QC H9J 2M5. July 2020.
8. Product monograph for Fraxiparine. Aspen Pharmacare Canada. Oakville, ON L6M 3E3. September 2019.
9. Product monograph for Innohep. Leo Pharma. Thornhill, ON L3T 7W8. May 2017.
10. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2022. http://www.clinicalkey.com. (Accessed May 11, 2022).
11. Akl EA, Kahale LA, Ballout RA, et al. Parenteral anticoagulation in ambulatory patients with cancer. Cochrane Database Syst Rev. 2014 Dec 10;(12):CD006652.
12. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e227S-e277S. Erratum in: Chest. 2012 May;141(5):1369.
13. Easaw JC, Shea-Budgell MA, Wu CM, et al. Canadian consensus recommendations on the management of venous thromboembolism in patients with cancer. Part 1: prophylaxis. Curr Oncol. 2015 Apr;22(2):133-43.
14. Thrombosis Canada. Thromboprophylaxis: non-orthopedic surgery. Revised January 31, 2022. https://thrombosiscanada.ca/wp-uploads/uploads/2022/02/8.-Thromboprophylaxis-Non-Ortho_31Jan2022.pdf. (Accessed May 11, 2022).
15. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest. 2021 Dec;160(6):e545-e608. doi: 10.1016/j.chest.2021.07.055.
16. Thrombosis Canada. Air travel-related thrombosis. Revised November 14, 2021. https://thrombosiscanada.ca/wp-uploads/uploads/2021/11/46.-Air-travel-related-Thrombosis_14Nov2021.pdf. (Accessed May 12, 2022).
17. Spyropoulos AC, Ageno W, Albers GW, et al. Rivaroxaban for Thromboprophylaxis after Hospitalization for Medical Illness. N Engl J Med. 2018 Sep 20;379(12):1118-1127.
18. Product monograph for Arixtra. Aspen Pharmacare Canada. Oakville, ON L6M 3E3. July 2019.
19. Marques MA, Panico MDB, Porto CLL, et al. Venous thromboembolism prophylaxis on flights. J Vasc Bras. 2018 Jul-Sep;17(3):215-219.
20. Schünemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. Blood Adv. 2018 Nov 27;2(22):3198-3225.
21. Product information for Xarelto. Janssen Pharm. Titusville, NJ 08560. January 2022.
22. CDC. Blood clots during travel. Page last reviewed October 23, 2017. https://wwwnc.cdc.gov/travel/page/dvt. (Accessed May 12, 2022).
23. American Heart Association. Know your risks for a dangerous blood clot. 2018. https://www.heart.org/-/media/files/health-topics/vte/vte_risk_checklist.pdf?la=en. (Accessed May 12, 2022).
24. National Blood Clot Alliance. Passport to safety.https://www.stoptheclot.org/wp-content/uploads/2016/07/Passport-to-Safety.pdf. (Accessed May 12, 2022).
25. ACOG Committee Opinion No. 746: Air Travel During Pregnancy. Obstet Gynecol. 2018 Aug;132(2):e64-e66. doi: 10.1097/AOG.0000000000002757.

Cite this document as follows: **Clinical Resource,** ***Venous Thromboembolism Prophylaxis. Pharmacist's Letter/Prescriber's Letter.*** **June 2022. [380604]**