

| Guideline Page and Request  | Panel Discussion/References  | Institution Vote |    |         |        |
|---|--|------------------|----|---------|--------|
|   |  | YES              | NO | ABSTAIN | ABSENT |
| <p><b>VTE-E, 1 of 5</b><br/>Internal request:<br/><u>Monotherapy Options</u><br/>Consider whether the recommendation for dalteparin as a single-agent treatment option for therapeutic anticoagulation for venous thromboembolism, with the following dosing details, is supported by high-level evidence:<br/>200 units/kg SC daily for 30 days, then 150 units/kg once daily for 2-6 months</p> | <p>Uniform panel consensus supported revising dalteparin to a category 1 treatment option for therapeutic anticoagulation.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Lee AYY, Levine MN, Baker RI, et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. <i>N Engl J Med</i> 2003;349:146-153.</li> <li>• Francis CW, Kessler CM, Goldhaber SZ, et al. Treatment of venous thromboembolism in cancer patients with dalteparin for up to 12 months: the DALTECAN Study. <i>J Thromb Haemost</i> 2015;13:1028-1035.</li> <li>• Prescribing information: Dalteparin sodium injection, for subcutaneous use; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf</a>.</li> </ul>  | 19               | 1  | 1       | 7      |
| <p><b>VTE-E, 1 of 5</b><br/>Internal request:<br/><u>Monotherapy Options</u><br/>Consider adding enoxaparin as a single-agent treatment option for therapeutic anticoagulation for venous thromboembolism, with the following dosing details:<br/>1 mg/kg SC every 12 hours.</p>  | <p>Uniform panel consensus supported adding enoxaparin as a category 2A treatment option for therapeutic anticoagulation.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Enoxaparin sodium injection for subcutaneous and intravenous use; 2013. Available at: <a href="http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf">http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf</a>.</li> <li>• Meyer G, Marjanovic Z, Valcke J, et al. Comparison of low-molecular-weight heparin and warfarin for the secondary prevention of venous thromboembolism in patients with cancer: a randomized controlled study. <i>Arch Intern Med</i> 2002;162:1729-1735.</li> <li>• Deitcher SR, Kessler CM, Merli G, et al. Secondary prevention of venous thromboembolic events in patients with active cancer: enoxaparin alone versus initial enoxaparin followed by warfarin for a 180-day period. <i>Clin Appl Thromb Hemost</i> 2006;12:389-396.</li> <li>• Merli G, Spiro TE, Olsson CG, et al. Subcutaneous enoxaparin once or twice daily compared with intravenous unfractionated heparin for treatment of venous thromboembolic disease. <i>Ann Intern Med</i> 2001;134:191-202.</li> </ul> | 21               | 0  | 0       | 7      |

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|---|--|------------------|----|---------|--------|
|   |  | YES              | NO | ABSTAIN | ABSENT |
| <p><b>VTE-E, 1 of 5</b><br/>Internal request:<br/><u>Monotherapy Options</u><br/>Consider adding fondaparinux as a single-agent treatment option for therapeutic anticoagulation for venous thromboembolism, with the following dosing details:<br/>5 mg [&lt;50 kg]; 7.5 mg [50–100 kg]; 10 mg [&gt;100 kg] SC daily.</p>  | <p>Uniform panel consensus supported adding fondaparinux as a category 2A treatment option for therapeutic anticoagulation.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Fondaparinux sodium solution for subcutaneous injection; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021345s035lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021345s035lbl.pdf</a>.</li> <li>• van Doormaal FF, Raskob GE, Davidson BL, et al. Treatment of venous thromboembolism in patients with cancer: subgroup analysis of the Matisse clinical trials. <i>Thromb Haemost</i> 2009;101:762-769.</li> </ul>         | 18               | 2  | 1       | 7      |
| <p><b>VTE-E, 1 of 5</b><br/>Internal request:<br/><u>Monotherapy Options</u><br/>Consider adding unfractionated heparin (UFH) as a single-agent treatment option for therapeutic anticoagulation for venous thromboembolism, with the following dosing options:</p> <ul style="list-style-type: none"> <li>• UFH IV then SC: IV 80 units/kg load, then 18 units/kg/h, target aPTT of 2–2.5 x control or per hospital SOPs, then SC 250 units/kg every 12 hours</li> <li>• UFH SC: SC 333 unit/kg load, then SC 250 units/kg every 12 hours</li> </ul> | <p>Nonuniform panel consensus supported adding unfractionated heparin (UFH) as a Category 2B treatment option.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Heparin sodium injection for intravenous or subcutaneous use; 2016. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017029s140lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017029s140lbl.pdf</a>.</li> <li>• Kearon C, Ginsberg JS, Julian JA, et al. Comparison of fixed-dose weight-adjusted unfractionated heparin and low-molecular-weight heparin for acute treatment of venous thromboembolism. <i>JAMA</i> 2006;296:935-942.</li> </ul> | 13               | 7  | 1       | 7      |

NCCN Guidelines for Cancer-Associated Venous Thromboembolic Disease (VTE) V.1.2018 – Follow-Up on 03/12/18

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|---|---|------------------|----|---------|--------|
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| <p><b>VTE-E, 2 of 5</b><br/>                     Internal request:<br/> <u>Combination Therapy Options</u><br/>                     Consider LMWH + warfarin, with the therapies listed under “LMWH + Warfarin options” (dalteparin + warfarin and enoxaparin + warfarin), is supported by high-level evidence as an option for therapeutic anticoagulation for venous thromboembolism.</p> | <p>There was nonuniform panel consensus that this recommendation was supported by high level evidence, so the recommendation for LMWH + warfarin for therapeutic anticoagulation is a category 2A treatment option.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Enoxaparin sodium injection for subcutaneous and intravenous use; 2013. Available at: <a href="http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf">http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf</a>.</li> <li>• Prescribing information: Dalteparin sodium injection, for subcutaneous use; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf</a>.</li> <li>• Palareti G, Legnani C, Lee A, et al. A comparison of the safety and efficacy of oral anticoagulation for the treatment of venous thromboembolic disease in patients with or without malignancy. <i>Thromb Haemost</i> 2000;84:805-810.</li> <li>• Hutten BA, Prins MH, Gent M, et al. Incidence of recurrent thromboembolic and bleeding complications among patients with venous thromboembolism in relation to both malignancy and achieved international normalized ratio: a retrospective analysis. <i>J Clin Oncol</i> 2000;18:3078-3083.</li> <li>• Prandoni P, Lensing AWA, Piccioli A, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. <i>Blood</i> 2002;100:3484-3488.</li> </ul> | 12               | 7  | 2       | 7      |
| <p><b>VTE-E, 2 of 5</b><br/>                     Internal request:<br/> <u>Combination Therapy Options</u><br/>                     Consider whether the recommendation for LMWH followed by edoxaban, as listed with dosing details under “Combinations with Edoxaban”, is supported by high-level evidence as an option for therapeutic anticoagulation for venous thromboembolism.</p>   | <p>Uniform panel consensus supported revising the recommendation for LMWH followed by edoxaban to a category 1 treatment option.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Dalteparin sodium injection, for subcutaneous use; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020287s069lbl.pdf</a>.</li> <li>• Prescribing information: Enoxaparin sodium injection for subcutaneous and intravenous use; 2013. Available at: <a href="http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf">http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020164s102lbl.pdf</a></li> <li>• Prescribing Information: Edoxaban tablets, for oral use; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206316s012lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206316s012lbl.pdf</a>.</li> <li>• Raskob GE, Es Nv, Verhamme P, et al. Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism. <i>New England Journal of Medicine</i> 2018;378:615-624.</li> </ul>   | 20               | 1  | 0       | 7      |

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|  |   | YES              | NO | ABSTAIN | ABSENT |
| <p><b>VTE-E, 2 of 5</b><br/>                     Internal request:<br/> <u>Combination Therapy Options</u><br/>                     Consider whether the recommendation for UFH followed by edoxaban, as listed with dosing details under “Combinations with Edoxaban”, is supported by high-level evidence as an option for therapeutic anticoagulation for venous thromboembolism.</p> | <p>There was nonuniform panel consensus that this recommendation was supported by high level evidence, so UFH followed by edoxaban remains a category 2A treatment option.</p> <p>Supporting References:</p> <ul style="list-style-type: none"> <li>• Prescribing information: Heparin sodium injection for intravenous or subcutaneous use; 2016. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017029s140lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017029s140lbl.pdf</a>.</li> <li>• Prescribing Information: Edoxaban tablets, for oral use; 2017. Available at: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206316s012lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206316s012lbl.pdf</a>.</li> <li>• Raskob GE, Es Nv, Verhamme P, et al. Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism. New England Journal of Medicine 2018;378:615-624.</li> </ul> | 15               | 4  | 2       | 7      |