



COMPENDIA TRANSPARENCY TRACKING FORM

DATE: August 25, 2020

PACKET: 1953

DRUG: Dalteparin

USE: Thromboembolism of vein - Prophylaxis; In high-risk outpatients, Malignant neoplastic disease

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: A, C, L, S *to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant advance over current therapies
C	Cancer or cancer-related condition
E	Quantity and robustness of evidence for use support consideration
L	Limited alternative therapies exist for condition of interest
P	Pediatric condition
R	Rare disease
S	Serious , life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]



EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
<p>Perry, JR, Julian, JA, Laperriere, NJ, et al: PRODIGE: a randomized placebo-controlled trial of dalteparin low-molecular-weight heparin thromboprophylaxis in patients with newly diagnosed malignant glioma. J Thromb Haemost Sep 2010; Vol 8, Issue 9; pp. 1959-1965.</p>	<p>This was an open-label, randomized-controlled trial that assessed dalteparin versus placebo for thromboprophylaxis in cancer patients at high risk for venous thromboembolism. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition and selective reporting were deemed low. Although the trial was open-label, the authors measured objective outcomes and employed a blinded central adjudication committee for outcome assessment. Of note, the trial had low accrual and was stopped early due to expiration of the study drug, which could bias the resulting estimates of treatment effect.</p>	<p>S</p>
<p>Maraveyas, A, Waters, J, Roy, R, et al: Gemcitabine versus gemcitabine plus dalteparin thromboprophylaxis in pancreatic cancer. Eur J Cancer Jun 2012; Vol 48, Issue 9; pp. 1283-1292.</p>	<p>This was an open-label, randomized-controlled trial that assessed the addition of dalteparin to gemcitabine for thromboprophylaxis in cancer patients at high risk for venous thromboembolism. The risk of potential bias associated with randomization, allocation concealment, performance, attrition and selective reporting were deemed low. The risk of detection bias was high due to the trial being open-label without an adjudication committee for VTE-related outcomes. The multiple protocol amendments could also introduce bias in the trial.</p>	<p>S</p>
<p>Khorana, AA, Francis, CW, Kuderer, NM, et al: Dalteparin thromboprophylaxis in cancer patients at high risk for venous thromboembolism: a randomized trial. Thromb Res Mar 2017; Vol 151, pp. 89-95.</p>	<p>This was an open-label, randomized-controlled trial that assessed dalteparin versus observation for thromboprophylaxis in cancer patients at high risk for venous thromboembolism. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition and selective reporting were deemed low. Although the trial was open-label, the authors measured objective outcomes and employed a blinded central adjudication committee for outcome assessment.</p>	<p>S</p>
<p>Krasinski, Z, Szpurek, D, Staniszewski, R, et al: The value of extended preoperative thromboprophylaxis with dalteparin in patients with ovarian cancer qualified to surgical treatment. Int Angiol Aug 2014; Vol 33, Issue 4; pp. 365-371.</p>		<p>4</p>



Farge, D, Frere, C, Connors, JM, et al: 2019 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol Oct 2019; Vol 20, Issue 10; pp. e566-e581.		S
Key, NS, Khorana, AA, Kuderer, NM, et al: Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. J Clin Oncol Aug 05, 2019; Vol Epub, p. Epub.		S
Khorana, AA, Francis, CW, Kuderer, N, et al: Dalteparin thromboprophylaxis in cancer patients at high risk for venous thromboembolism: A randomized trial. Blood Dec 03, 2015; Vol 126, Issue 23; p. 427.		4

Literature evaluation codes: **S** = Literature selected; **1** = Literature rejected = Topic not suitable for scope of content; **2** = Literature rejected = Does not add clinically significant new information; **3** = Literature rejected = Methodology flawed/Methodology limited and unacceptable; **4** = Other (review article, letter, commentary, or editorial)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Cynthia Beckett, PharmD	None		
Margi Schiefelbein, PA	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.



ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use Dalteparin in various clinical trials does appear to be somewhat effective in reducing VTE in some cancer types. The risk of serious bleeding must be taken into consideration though.	
John Roberts	Ineffective	Class III: Not Recommended	Several agents other than dalteparin have shown some efficacy and acceptable safety in the prevention of venous thromboembolism in patients with diverse kinds of cancers and receiving diverse types of treatments. Most studies of dalteparin in these situations have not shown overall benefit and some suggest harm. In a randomized trial in patients with pancreas cancer receiving gemcitabine only hemotherapy, dalteparin did reduce the frequency of venous thromboembolism without increasing the frequency of bleeding. This specific situation is uncommon, however; regardless and other more generally useful agents should be preferred.	
Richard LoCicero	Effective	Class IIa: Recommended, in Most Cases	Clinical trials have established the efficacy of dalteparin (a low molecular weight heparin) for the prevention of thromboembolism in patients with cancer. Consensus, evidence-based guidelines are published by both the America Society of Clinical Oncology, and the International Initiative on Thrombosis and Cancer supporting this practice. This appears to be a class effect and there are several low molecular heparins that are commercially available. Dalteparin is one of them.	