TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 10/16/2018

PACKET: 1721

DRUG: Enoxaparin Sodium

USE: Treatment of venous thromboembolism in patients with cancer

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: C *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)]

TRUVEN HEALTH ANALYTICS
an IBM Company

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Akl EA et al. Low molecular weight heparin versus unfractionated heparin for perioperative thromboprophylaxis in patients with cancer. Cochrane Database Syst.Rev. Jun 26, 2014; Issue 6; p. CD009447	Comments: This was a Cochrane systematic review which included randomized controlled trials comparing low molecular weight heparin (LMWH) and Vitamin K antagonist (VKA) for the long-term treatment of venous thromboembolism (VTE) in patients with cancer. Ten randomized trials and 1981 individuals were included. The risk of bias tool was used to assess the quality of the included trials. Overall, the risk of bias was judged to be high for performance bias, and low for selection bias, detection bias, attrition bias, reporting bias, and other potential sources of bias. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	1
Akl EA et al: Anticoagulation for the long-term treatment of venous thromboembolism in patients with cancer. Cochrane Database Syst Rev. Jul 08, 2014; Vol 2014, Issue 7; p. CD006650.	Comments: This was a Cochrane systematic review which included randomized controlled trials comparing unfractionated heparin (UFH) and low molecular weight heparin (LMWH) in people with cancer planning to undergo a surgical intervention. Sixteen randomized trials and 12890 individuals were included. The risk of bias tool was used to assess the quality of the included trials. Overall, the risk of bias was judged to be unclear for slection bias and low for detection bias, attrition bias, reporting bias, and other potential sources of bias. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	S
Hakoum MB et al. Anticoagulation for the initial treatment of venous thromboembolism in people with cancer. Cochrane Database Syst Rev. Jan 24, 2018; Vol 2018, Issue 1; p. CD006649.	Comments: This was a Cochrane systematic review which included randomized controlled trials comparing unfractionated heparin (UFH), low molecular weight heparin (LMWH), and fondaparinux for the initial treatment of venous thromboembolism (VTE) in patients with cancer. Fifteen randomized trials and 1615 individuals were included. The risk of bias tool was used to assess the quality of the included trials. Overall, the risk of bias was judged to be high for performance bias, and low for selection bias, detection bias, attrition bias, reporting bias, and other potential sources of bias. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	S

Couturaud,F et al. Low molecular weight heparin administered once versus twice daily in patients with venous thromboembolism: a meta-analysis. Thromb Haemost Oct 2001; Vol 86, Issue 4; pp. 980-984.	Comments: This was a systematic review which included randomized controlled trials comparing once-daily and twice-daily low molecular weight heparin (LMWH) in people with thrombosis. Five randomized trials and 1552 individuals were included. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	1
Merli G et al: Subcutaneous enoxaparin once or twice daily compared with intravenous unfractionated heparin for treatment of venous thromboembolic disease. Ann Intern Med Feb 06, 2001; Vol 134, Issue 3; pp. 191-202.	Comments: This was a partially blinded, randomized clinical trial that studied deep venous thrombosis in 900 cancer patients. The risk of potential bias associated with randomization, allocation concealment, blinding, attrition, and reporting were all deemed low.	2
Pelzer U et al: Efficacy of prophylactic low-molecular weight heparin for ambulatory patients with advanced pancreatic cancer: outcomes from the CONKO-004 trial. J Clin Oncol Jun 20, 2015; Vol 33, Issue 18; pp. 2028-2034.	Comments: This was an open-label, randomized clinical trial that studied venous thromboembolic events in 312 advanced pancreatic cancer patients. The risk of potential bias associated with randomization, outcome assessment, attrition, and reporting were deemed low. The risk of potential bias for allocation concealment was deemed high due to the open-label design.	1
Meyer,G 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. Arch Intern Med Aug 12, 2002; Vol 162, Issue 15; pp. 1729-1735.	Comments: This was an open-label, randomized clinical trial that studied venous thromboembolic events in 146 cancer patients. One caveat of the study is the fact that it was powered for 120 patients in each arm, but enrollment was stopped early due to slow recruitment. The risk of potential bias associated with randomization, outcome assessment, attrition, and reporting were deemed low. The risk of potential bias for allocation concealment and blinding were deemed high due to the open-label design.	2

Deitcher SR 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. Clin Appl.Thromb.Hemost Oct 2006; Vol 12, Issue 4; pp. 389-396.	Comments: This was an open-label, randomized clinical trial that studied venous thromboembolic events in 102 cancer patients. A major caveat of this study is the open-label design and lack of independent reviewers. The risk of potential bias associated with randomization, attrition, and reporting were deemed low. The risk of potential bias for allocation concealment, blinding, and outcome assessment were deemed high due to the open-label design.	2
Diaz,A.H., Rodgers,G.M., and Gilreath,J.A.: Enoxaparin once daily vs. twice daily dosing for the treatment of venous thromboembolism in cancer patients: A literature summary. Journal of Oncology Pharmacy Practice 2012; Vol 18, Issue 2; pp. 264-270.		4
Farge,D., Debourdeau,P., Beckers,M., et al: International clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. J Thromb.Haemost Jan 2013; Vol 11, Issue 1; pp. 56-70.		4
Farge,D., Bounameaux,H., Brenner,B., et al: International clinical practice guidelines including guidance for direct oral anticoagulants in the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol Oct 2016; Vol 17, Issue 10; pp. e452-e466.		4

Frere,C. and Farge,D.: Clinical practice guidelines for prophylaxis of venous thomboembolism in cancer patients. Thromb.Haemost. Sep 27, 2016; Vol 116, Issue 4; pp. 618-625.		4
Kearon,C., Akl,E.A., Comerota,A.J., et al: Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest Feb 2012; Vol 141, Issue 2 Suppl; pp. e419S-e494S.		4
Lyman,G.H., Khorana,A.A., Kuderer,N.M., et al: Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol Jun 10, 2013; Vol 31, Issue 17; pp. 2189-2204.		S
Lyman,G.H., et al: Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update 2014. J Clin Oncol 2015 Feb 20;33(6):654-6		S

Sibson,K.R., Biss,T.T., Furness,C.L., et al: BSH Guideline: management of thrombotic and haemostatic issues in paediatric malignancy. Br.J Haematol. Feb 2018; Vol 180, Issue 4; pp. 511-525.		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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	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
MICROMEDEX	Effective	Class I: Recommended		B
John D Roberts	Effective	Class IIa: Recommended, in Most Cases	Multiple trials have shown enoxaparin to be superior to unfractionated heparin and warfarin in the immediate and long term management, respectively, of deep venous thrombosis in patients with cancer. Enoxaparin is contraindicated in patients with a creatinine clearance < 30.	N/A
Jeffrey Klein	Evidence Favors Efficacy	Class I: Recommended	The use of enoxaparin to treat venous thromboembolism in patients with cancer appears to be safe and effective over hepain or the newer anticoagulants that have entered the marketplace. Unfortunately two of the three studies did not mention enoxaparin by name, instead the class of LMWH were referenced. Enoxaparin is a member of the LMWH group	N/A

Richard LoCicero	Effective	Class I: Recommended	Extensive clinical trial data supports the use of enoxaparin in the treatment of venous thromboembolism in patients with cancer. Specifically, it may be more effective than vitamin K antiagonists, without increased toxicity.	N/A