



**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** 05/14/2021

**PACKET:** 2085

**DRUG:** Bevacizumab

**USE:** Nonsquamous nonsmall cell neoplasm of lung; Stage IIIB/IV, continuation maintenance therapy as a single-agent following platinum-based, first-line therapy

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, S \*to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant <b>advance</b> over current therapies
C	<b>Cancer</b> or cancer-related condition
E	Quantity and robustness of <b>evidence</b> for use support consideration
L	<b>Limited</b> alternative therapies exist for condition of interest
P	<b>Pediatric</b> condition
R	<b>Rare</b> disease
S	<b>Serious</b> , 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
Akamatsu, H, Ninomiya, K, Kenmotsu, H, et al: The Japanese Lung Cancer Society Guideline for non-small cell lung cancer, stage IV. Int J Clin Oncol Jul 2019; Vol 24, Issue 7; pp. 731-770.		2
Planchard, D, Popat, S, Kerr, K, et al: Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Oct 01, 2018; Vol 29, Issue Suppl 4; pp. iv192-iv237.		S
Hanna N, Johnson D, Temin S, et al: Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline Update. J Clin Oncol 2017; 35(30):3484-3515.		S
Ramalingam, SS, Dahlberg, SE, Belani, CP, et al: Pemetrexed, Bevacizumab, or the Combination As Maintenance Therapy for Advanced Nonsquamous Non-Small-Cell Lung Cancer: ECOG-ACRIN 5508. J Clin Oncol Sep 10, 2019; Vol 37, Issue 26; pp. 2360-2367.	This was an open-label, Phase III randomized trial that investigated bevacizumab, pemetrexed, and their combination for maintenance therapy in people with advanced nonsquamous non-small-cell lung cancer. The risk of potential bias associated with randomization, detection, attrition, and reporting were deemed low. The risk of potential bias that could result from not rigorously implementing allocation concealment was unclear due to the lack of information on these methods. Performance bias was deemed high risk due to the open-label nature of the study; however detection bias was deemed low due to the use of survival as the primary outcome.	S



<p>Seto, T, Azuma, K, Yamanaka, T, et al: Randomized Phase III Study of Continuation Maintenance Bevacizumab With or Without Pemetrexed in Advanced Nonsquamous Non-Small-Cell Lung Cancer: COMPASS (WJOG5610L). J Clin Oncol Mar 10, 2020; Vol 38, Issue 8; pp. 793-803.</p>		2
<p>Barlesi, F, Scherpereel, A, Rittmeyer, A, et al: Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). J Clin Oncol Aug 20, 2013; Vol 31, Issue 24; pp. 3004-3011.</p>		2
<p>Barlesi, F, Scherpereel, A, Gorbunova, V, et al: Maintenance bevacizumab-pemetrexed after first-line cisplatin-pemetrexed-bevacizumab for advanced nonsquamous nonsmall-cell lung cancer: updated survival analysis of the AVAPERL (MO22089) randomized phase III trial. Ann Oncol May 2014; Vol 25, Issue 5; pp. 1044-1052.</p>		2
<p>Karayama, M, Inui, N, Fujisawa, T, et al: Maintenance therapy with pemetrexed and bevacizumab versus pemetrexed monotherapy after induction therapy with carboplatin, pemetrexed, and bevacizumab in patients with advanced non-squamous non small cell lung cancer. Eur J Cancer May 2016; Vol 58, pp. 30-37.</p>		3



Yoshida, H, Kim, YH, Sakamori, Y, et al: A Randomized Phase II Study of Maintenance Bevacizumab, Pemetrexed or Bevacizumab Plus Pemetrexed for Advanced Non-squamous Non-small Cell Lung Cancer. Anticancer Res May 2020; Vol 40, Issue 5; pp. 2981-2987.		3
Hanna, N and Jalal, S: The Case for Maintenance Pemetrexed Plus Bevacizumab. J Clin Oncol Mar 01, 2020; Vol 38, Issue 7; pp. 770-771.		4
Ramalingam, SS and Dahlberg, SE: Reply to N. Hanna et al and L. Xie et al. J Clin Oncol Mar 01, 2020; Vol 38, Issue 7; pp. 771-772.		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		
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

	<b>EFFICACY</b>	<b>STRENGTH OF RECOMMENDATION</b>	<b>COMMENTS</b>	<b>STRENGTH OF EVIDENCE</b>
<b>IBM MICROMEDEX</b>	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Bevacizumab as a single maintenance agent in NSCLC patients has a strong overall response. The toxicity of bevacizumab must be considered especially those patients who have other comorbidities. There are other single agents on the market as well that might have less adverse effects	
John Roberts	Evidence Favors Efficacy	Class III: Not Recommended	Pemetrexed maintenance therapy following platinum-based first-line therapy without progression of disease has been shown to modestly prolong overall survival in advanced nonsquamous nonsmall cell lung cancer. In a subsequent trial bevacizumab maintenance was been shown to be similar to pemetrexed maintenance (Ramalingam et al. J Clin Oncol 37:2360-2367). This study is not sufficient to recommend bevacizumab as an alternative to pemetrexed, however, as pemetrexed was nominally superior to bevacizumab, and no non-inferiority analysis is presented.	
Richard LoCicero	Effective	Class I: Recommended	Randomized clinical trials have established the efficacy of maintenance bevacizumab after platinum-based chemotherapy in metastatic nonsquamous, nonsmall cell lung cancer with acceptable toxicity. Evidence-based consensus guidelines support this treatment as well.	