



COMPENDIA TRANSPARENCY TRACKING FORM

DATE: July 6, 2021

PACKET: 2117

DRUG: Pemetrexed

USE: Nonsquamous nonsmall cell neoplasm of lung; Stage IIIB/IV or recurrent, continuation maintenance therapy in combination with bevacizumab 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, L, E, 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
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.		4
Passiglia, F, Pilotto, S, Facchinetti, F, et al: Treatment of advanced non-small-cell lung cancer: The 2019 AIOM (Italian Association of Medical Oncology) clinical practice guidelines. Crit Rev Oncol Hematol Feb 2020; Vol 146, p. 102858.		4
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
Patel,J.D., Socinski,M.A., Garon,E.B., et al: PointBreak: a randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. Journal of Clinical Oncology Dec 01, 2013; Vol 31, Issue 34; pp. 4349-4357.		1



<p>Spigel,D.R., Patel,J.D., Reynolds,C.H., et al: Quality of life analyses from the randomized, open-label, phase III PointBreak study of pemetrexed-carboplatin-bevacizumab followed by maintenance pemetrexed-bevacizumab versus paclitaxel-carboplatin-bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. J Thorac Oncol Feb 2015; Vol 10, Issue 2; pp. 353-359.</p>		1
<p>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.</p>		1
<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>	<p>This was an open-label, Phase III randomized trial that investigated bevacizumab, with or without pemetrexed, 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.</p>	S



<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>	<p>This was an open-label, Phase III randomized trial that investigated bevacizumab, with or without pemetrexed, for maintenance therapy in patients with advanced nonsquamous non-small-cell lung cancer. The risk of potential bias associated with randomization, allocation concealment, and attrition were deemed low. The risk of performance and detection bias were deemed high because the authors employed an open-label design without centrally assessed outcomes. Selective outcome reporting was also deemed high risk due to the use of PFS as the primary outcome without centrally assessed response.</p>	<p>S</p>
<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>		<p>S</p>
<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>		<p>3</p>
<p>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.</p>		<p>3</p>



<p>Kondo, T, Kasai, T, Mori, K, et al: Randomized phase II trial of pemetrexed with or without bevacizumab maintenace after displatin, pemetrexed and bevacizumab in advanced non-squamous, non-small lung cancer (TORG1321). Ann Oncol 2020; Vol 31 Suppl 44, p. S875.</p>		<p>1</p>
---	--	----------

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 Roberts	None
		Todd Gersten	None
		Richard LoCicero	<p>Incyte Corporation</p> <p>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.</p>



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
Todd Gersten	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The prevailing evidence indicates that there exists a several month progression free survival benefit for the addition of pemetrexed to bevacizumab. Further, although not clinically significant in terms of an overall survival benefit, the data does suggest a trend toward an overall survival benefit.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Phase III clinical trials have demonstrated improved progression free survival when pemetrexed is added to bevacizumab as maintenance therapy for treatment of nonsquamous, nonsmall cell lung cancer. Overall survival benefit has not been established. In some cases, the risk/benefit ratio of this therapy may justify pemetrexed/bevacizumab maintenance therapy.	
John Roberts	Evidence is Inconclusive	Class IIb: Recommended, in Some Cases	In two randomized trials addition of pemetrexed to bevacizumab for maintenance therapy following platinum-based first-line therapy resulted in very modest improvement in disease free survival and no significant improvement in overall survival. Additional toxicity was moderate. Enrollment was limited to PS 0-1 with few exceptions. The risk-benefit ratio is modest at best. Further, most of these patients probably should be considered for immune checkpoint inhibitor therapy.	