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COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 7/12/16

PACKET: 1328

DRUG: Bevacizumab

USE: Nonsquamous nonsmall cell neoplasm of lung Stage IIIB/IV, first-line therapy in combination with pemetrexed and carboplatin

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, 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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Patel,J.D., 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.	Comments: This was a multicenter, randomized, open-label, phase III study. The risk of bias associated with an open-label design is low for objective outcomes, which include the primary endpoint, and it may be high for the subjective outcomes. There was low risk of bias associated with incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Spigel,D.R., 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.		S

Villaruz,L.C., et al: The occurrence of grade 4 adverse events and survival outcomes in patients with nonsquamous non-small cell lung cancer receiving bevacizumab with chemotherapy in the phase III PointBreak and AVAiL studies. Journal of Clinical Oncology 2013; Vol 31, Issue 15 SUPPL. 1; p. e19022.		2
Masters,G.A., et al: Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol Oct 20, 2015; Vol 33, Issue 30; pp. 3488-3515.		S
Socinski,M.A., et al: Treatment of stage IV non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest May 2013; Vol 143, Issue 5 Suppl; pp. e341S-e368S.		2

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		
		Jeffrey Klein	None
		John Roberts	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	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	In one trial provided the addition of bevacizumab to specifically pemetrexed and carboplatin showed some favorable results especially in those that did not have any contraindications for its use. The other trials provided did not "study" the specific combination of those 3 meds.	N/A

John Roberts	Ineffective	Class lll: Not Recommended	The combination of bevacizumab/carboplatin/paclitaxel yielded a modest survival benefit and significantly more toxicity compared to carboplatin/paclitaxel in a large randomized phase III trial. Although the triple drug combination was FDA approved on the basis of that study, in this reviewer's opinion implementation of this combination in clinical practice is likely to yield more harm than good. It is not recommended. Now, new data indicate that bevacizumab/carboplatin/pemetrexed is quite similar to bevacizumab/carboplatin/paclitaxel. As this reviewer does not recommend the latter combination, they do not recommend the former.	N/A
Richard LoCicero	Evidence is Inconclusive	Class llb: Recommended, In Some Cases	Clinical trial data presented supports the use of bevacizumab in combination with Carboplatin/Pemetrexed as a safe treatment option in stage IIIB/IV non-squamous non-small cell lung cancer. No data presented indicates the combination is harmful or decreases the effectiveness off Carbo/Pemetrexed alone.	N/A