TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Bevacizumab

INDICATION: Colon cancer, adjuvant therapy in combination with fluorouracil, leucovorin, and oxaliplatin

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, 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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Allegra,C.J., et al: Phase III trial assessing bevacizumab in stages II and III carcinoma of the colon: results of NSABP protocol C-08. J Clin Oncol Jan 01, 2011; Vol 29, Issue 1; pp. 11-16.	Study methodology comments: This was a randomized, open-label, multicenter, comparative trial. Additional strengths of the study included: 1) had both inclusion and exclusion criteria; 2) defined primary and secondary outcomes; 3) defined endpoint; 4) explained method of randomization; 5) conducted power analysis; 6) provided 95% confidence intervals; 7) compared baseline characteristics of groups; 8) controlled for the effect of confounding factors on outcomes; 9) defined exploratory analyses; and 10) made statistical adjustments to preserve the type 1 error rate. Weaknesses of the study included: 1) possible selection bias since subjects were not recruited randomly or consecutively; and 2) open-label design without the use of independent reviewers.	S
Allegra CJ, et al: Initial safety report of NSABP C-08: A randomized phase III study of modified FOLFOX6 with or without bevacizumab for the adjuvant treatment of patients with stage II or III colon cancer. J Clin Oncol 27:3385-3390, 2009.	Study methodology comments: This is the same study as above with a focus on safety data.	S
Allegra CJ., et al. Initial safety report of NSABP C-08, a randomized phase III study of modified 5-fluorouracil (5-FU)/leucovorin (LCV) and oxaliplatin (OX) (mFOLFOX6) with or without bevacizumab (bev) in the adjuvant treatment of patients with stage II/III colon cancer. 2008 ASCO Annual Meeting. Abstract.	Study methodology comments: Abstract	3

Tournigand C., et al. mFOLFOXbevacizumab or XELOX-bevacizumab then bevacizumab (B) alone or with erlotinib (E) in first-line treatment of patients with metastatic colorectal cancer (mCRC): Interim safety analysis of DREAM study. 2009 ASCO meeting abstract.	Study methodology comments: Abstract	3
Wolmark N, et al. A phase III trial comparing mFOLFOX6 to mFOLFOX6 plus bevacizumab in stage II or III carcinoma of the colon: Results of NSABP Protocol C-08. 2009 ASCO Annual Meeting. Abstract.	Study methodology comments: Abstract	3
Smith D., et al. Effectiveness of bevacizumab (BV) plus chemotherapy in first-line therapy of metastatic colorectal cancer (mCRC): Results of ETNA, a French cohort study. 2010 Gastrointestinal Cancers Symposium. Abstract	Study methodology comments: Abstract	3
Baek J., et al. The impact of deficient mismatch repair in patients with stage II or III colorectal cancer who were treated with adjuvant FOLFOX or XELOX. 2010 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3
Bendell JC, et al. Axitinib or bevacizumab (bev) plus FOLFOX or FOLFIRI as second-line therapy in patients (pts) with metastatic colorectal cancer (mCRC). 2011 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3

De Gramont A, et al. AVANT: Results from a randomized, three-arm multinational phase III study to investigate bevacizumab with either XELOX or FOLFOX4 versus FOLFOX4 alone as adjuvant treatment for colon cancer. 2011 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3
Infante JR, et al. A randomized phase II study comparing mFOLFOX-6 combined with axitinib or bevacizumab or both in patients with metastatic colorectal cancer (mCRC). 2011 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3
Arnold D. et al. Patterns of maintenance treatment (Tx) following first-line bevacizumab (bev) plus chemotherapy (CT) for metastatic colorectal cancer (mCRC): Results from a large German community-based cohort study. 2011 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3
Miura K, et al. A phase II multicenter trial of neoadjuvant chemotherapy FOLFOX6 in combination with bevacizumab for patients with resectable synchronous liver metastases after R0-resections of primary colorectal cancers: The interim analysis. 2011 Gastrointestinal Cancers Symposium. Abstract.	Study methodology comments: Abstract	3

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)

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CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	Jeffrey A. Bubis, DO	None
Felicia Gelsey, MS	None	Jeffrey F. Patton, MD	None
		Keith A. Thompson, MD	None
		James E. Liebmann, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward P. Balaban, DO	Ineffective	Class lll: Not Recommended	Really feel NSABP data warrants a "non-recommendation."	N/A
Jeffrey A. Bubis, DO	Ineffective	Class lll: Not Recommended	The available data does not demonstrate a clinically meaningful improvement in outcomes, but pts receiving Avastin had significantly higher toxicity.	N/A
Jeffrey F. Patton, MD	Ineffective	Class lll: Not Recommended	None	N/A
Keith A. Thompson, MD	Evidence is Inconclusive	Class lll: Not Recommended	None	N/A

James E. Liebmann, MD	Evidence is Inconclusive	Class lll: Not Recommended	Both papers reach the same, correct, conclusion. “Bevacizumab should not be used for the management of patients with stages ll and lll colon cancer in the adjuvant setting.” The only intriguing finding is the delay in tumor relapse possibly due to prolonged use of Bevacizumab. This finding, however, does not justify the use of the drug in this setting.	N/A