COMPENDIA TRANSPARENCY TRACKING FORM

DATE: May 11, 2022

OFF-LABEL ID #: 2181

DRUG NAME: Bevacizumab

OFF-LABEL USE: Malignant neoplasm of endometrium of corpus uteri – Advanced or recurrent

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, R, 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
Santaballa, A, Matias-Guiu, X, Redondo, A, et al: SEOM clinical guidelines for endometrial cancer (2017). Clin Transl Oncol Jan 2018; Vol 20, Issue 1; pp. 29-37.		4
Chen, H, Liang, M, and Min, J: Efficacy and safety of bevacizumab-combined chemotherapy for advanced and recurrent endometrial cancer: a systematic review and meta-analysis. Balkan Med J Jan 2021; Vol 38, Issue 1; pp. 7-12.		3
Aghajanian, C, Filiaci, V, Dizon, DS, et al: A phase II study of frontline paclitaxel/ carboplatin/ bevacizumab, paclitaxel/ carboplatin/ temsirolimus, or ixabepilone/ carboplatin/ bevacizumab in advanced/recurrent endometrial cancer. Gynecol Oncol Aug 2018; Vol 150, Issue 2; pp. 274-281.	This was a multicenter, randomized phase 2 clinical trial that investigated three different treatment regimens in patients with advanced or recurrent endometrial cancer. The randomized arms were then compared to historical controls from the GOG209 clinical trial. The risk of bias due to confounding and measurement of outcome were deemed moderate risk. The risk of bias associated with selection, classification of and deviation from intervention, missing data, and selective reporting were deemed low risk. A major caveat of the study is the lack of a concurrent control group.	S
Lorusso, D, Ferrandina, G, Colombo, N, et al: Carboplatin-paclitaxel compared to Carboplatin-Paclitaxel-Bevacizumab in advanced or recurrent endometrial cancer: MITO END-2 - a randomized phase II trial. Gynecol Oncol Dec 2019; Vol 155, Issue 3; pp. 406-412.	This was an open-label, randomized-controlled trial that compared carboplatin-paclitaxel, with or without bevacizumab, in patients with recurrent or advanced endometrial cancer. The risk of potential bias associated with randomization, allocation concealment, performance, attrition and reporting was deemed low. The risk of detection bias was deemed moderate risk due to the lack of independent central outcome review.	S

Aghajanian, C, Sill, MW, Darcy, KM, et al: Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol Jun 01, 2011; Vol 29, Issue 16; pp. 2259-2265.	This was a multicenter, single-arm, phase 2 clinical trial that investigated bevacizumab monotherapy in patients with recurrent or persistent endometrial cancer. The risk of bias due to measurement of outcome were deemed moderate risk. The risk of bias associated with confounding, selection, classification of and deviation from intervention, missing data, and selective reporting were deemed low risk. A major caveat of the study is the lack of a concurrent control group.	S
Alvarez, EA, Brady, WE, Walker, JL, et al: Phase II trial of combination bevacizumab and temsirolimus in the treatment of recurrent or persistent endometrial carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol Apr 2013; Vol 129, Issue 1; pp. 22-27.		1
Simpkins, F, Drake, R, Escobar, PF, et al: A phase II trial of paclitaxel, carboplatin, and bevacizumab in advanced and recurrent endometrial carcinoma (EMCA). Gynecol Oncol Feb 2015; Vol 136, Issue 2; pp. 240-245.		3
Rubinstein, MM, Dickinson, S, Narayan, P, et al: Bevacizumab in advanced endometrial cancer. Gynecol Oncol Jun 2021; Vol 161, Issue 3; pp. 720-726.		3
Rose, PG, Ali, S, Moslemi-Kebira, M, et al: Paclitaxel, carboplatin, and bevacizumab in advanced and recurrent endometrial carcinoma. Int J Gynecol Cancer Mar 2017; Vol 27, Issue 3; pp. 452-458.		2

Wright JD, Powell MA, Rader JS, Mutch DG, Gibb RK. Bevacizumab therapy in patients with recurrent uterine neoplasms. Anticancer Res. 2007 Sep-Oct;27(5B):3525-8.		2
Concin N, . ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Radiother Oncol. 2021 Jan;154:327-353. PMID: 33712263.		S

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
		Todd Gersten	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
IBM MICROMEDEX	Evidence is Inconclusive	Class III: Not Recommended		B
John Roberts	Evidence is Inconclusive	Class III: Not Recommended	A single, small randomized trial of carboplatin/paclitaxel without or with bevacizumab in advanced or recurrent endometrial cancer showed no convincing benefit and moderate toxicity. Other single arm trials show modest activity in terms of response rates and confirm moderate toxicity. Use outside of a clinical trial is not recommended.	
Todd Gersten	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The prevailing presented data is most robust when bevacizumab is used in combination with chemotherapy. When used with chemotherapy in the advanced/recurrence disease setting, strong trends and statistically beneficial improvements are seen in overall survivorship.	
Richard LoCicero	Evidence is Inconclusive	Class III: Not Recommended	Three phase II trials (2 randomized and 1 single arm) have evaluated the efficacy of bevacizumab in the treatment of advanced or recurrent endometrial cancer. Neither of the 2 randomized trial established efficacy of the addition of bevacizumab to chemotherapy. The single arm trial identified clinical effect without unexpected toxicity. At this time, there is inadequate clinical trial data to support the use of bevacizumab in this setting.	