COMPENDIA TRANSPARENCY TRACKING FORM

DATE: May 18, 2022

OFF-LABEL ID #: 2187

DRUG NAME: Lenvatinib

OFF-LABEL USE: Malignant neoplasm of endometrium of corpus uteri; Advanced disease, dMMR, in combination with pembrolizumab in patients with disease progression following prior chemotherapy

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, *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
Concin, N, Matias-Guiu, X, Vergote, I, et al: ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int J Gynecol Cancer Jan 2021; Vol 31, Issue 1; pp. 12-39.		4
Makker, V, Colombo, N, Casado Herraez, A, et al: Lenvatinib plus Pembrolizumab for Advanced Endometrial Cancer. N Engl J Med Feb 03, 2022; Vol 386, Issue 5; pp. 437-448.	This was an open-label, active comparator, randomized clinical trial that investigated lenvatinib and pembrolizumab combination treatment in advanced endometrial cancer patients. The risk of bias associated with randomization, allocation concealment, performance, detection, attrition and reporting were all deemed low.	S
Vergote, I, Powell, MA, Teneriello, MG, et al: Second-line lenvatinib in patients with recurrent endometrial cancer. Gynecol Oncol Mar 2020; Vol 156, Issue 3; pp. 575-582.		1
Makker, V, Taylor, MH, Aghajanian, C, et al: Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer. J Clin Oncol Sep 10, 2020; Vol 38, Issue 26; pp. 2981-2992.		2

Marth, C, Tarnawski, R, Tyulyandina, A, et al: Phase 3, randomized, open-label study of pembrolizumab plus lenvatinib versus chemotherapy for first-line treatment of advanced or recurrent endometrial cancer: ENGOT-en9/LEAP-001. Int J Gynecol Cancer Jan 2022; Vol 32, Issue 1; pp. 93-100.		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		
		Howard Goodman	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

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases		B

Howard Goodman	Effective	Class I: Recommended	The treatment for patients with recurrent endometrial cancer not amenable to potentially curable radiation therapy, has been limited to cytotoxic chemotherapy or hormonal therapies. The advent of immunotherapy agents has added to the ability to treat. Current study well summarized. Randomized trial studying combination of Pembro/lenvatinib in women with recurrent endometrial carcinoma. Stratified by MMR status, both groups benefit. In the dMMR subgroup, overall response rate, median survival, overall survival all showed statistically significant benefit. Median overall survival not reached in the study group. On this basis this combination may be recommended. There are other studies showing improvement with pembro alone in th dMMR group. No comments can be made re benefit of the combination vs single agent pembro as his was not studied in this paper.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Lenvatinib with Pembrolizumab in advanced endometrial cancer patients demonstrated a higher degree of progression free survival, as well as higher survival overall when compared to chemotherapy alone. However the degree of more serious adverse effects with the non chemotherapy regimen was higher than with the chemotherapy regimen.	
Richard LoCicero	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The combination of pembrolizumab and lenvatinib in treatment of advanced endometrial cancer had superior progression-free survival and overall survival vs. chemotherapy (doxorubicin or paclitaxel) in patients with deficient mismatch repair; in a randomized trial. Unexpected toxicity was not observed.	