COMPENDIA TRANSPARENCY TRACKING FORM

DATE: August 11, 2022

OFF-LABEL ID #: 2417

DRUG NAME: Pembrolizumab

OFF-LABEL USE: Malignant tumor of anus; Advanced or metastatic squamous cell disease, previously treated

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
Stewart, DB, Gaertner, WB, Glasgow, SC, et al: The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for Anal Squamous Cell Cancers (Revised 2018). Dis Colon Rectum Jul 2018; Vol 61, Issue 7; pp. 755-774.		1
Rao, S, Guren, MG, Khan, K, et al: Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Sep 2021; Vol 32, Issue 9; pp. 1087-1100.		S
Moureau-Zabotto, L, Vendrely, V, Abramowitz, L, et al: Anal cancer: French Intergroup Clinical Practice Guidelines for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SNFCP). Dig Liver Dis Aug 2017; Vol 49, Issue 8; pp. 831-840.		1
Marabelle, A, Cassier, PA, Fakih, M, et al: Pembrolizumab for previously treated advanced anal squamous cell carcinoma: results from the non-randomised, multicohort, multicentre, phase 2 KEYNOTE-158 study. Lancet Gastroenterol Hepatol May 2022; Vol 7, Issue 5; pp. 446-454.	This was a prospective multicenter mutliple cohort phase 2 trial that investigated pembrolizumab treatment in patients with treatment-refractory metastatic anal cancer. The risk of bias due to unmeasured confounders, selection of participants, classification of intervention, deviation from intervention, missing data, measurement of outcome, and selective reporting were deemed low risk. No other sources of bias were found.	S

Ott, PA, Piha-Paul, SA, Munster, P, et al: Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. Ann Oncol May 01, 2017; Vol 28, Issue 5; pp. 1036-1041.	This was a prospective multicenter multiple cohort phase Ib study that investigated pembrolizumab treatment in patients with locally advanced or metastatic anal cancer. The risk of bias due to unmeasured confounders, selection of participants, classification of intervention, deviation from intervention, missing data, and selective reporting were deemed low risk. The risk of bias associated with measurement of outcome was deemed moderate risk due to lack of central outcome assessment. No other sources of bias were found.	S
Spehner, L, Boustani, J, Cabel, L, et al: Present and Future Research on Anal Squamous Cell Carcinoma. Cancers (Basel) Aug 02, 2021; Vol 13, Issue 15; p. 3895.		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		
		Todd Gersten	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 IIb: Recommended, in Some Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of Pembrolizumab as monotherapy in previously treated advanced or metastatic squamous cell disease, demonstrated a promising overall survival. The safety profile was generally favorable and manageable. Specific patient types it appears should probably only be part of this treatment (PDL1+), as those patients tend to respond better.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	A phase Ib and a phase II trial have demonstrated the efficacy of pembrolizumab in the second line therapy for advanced or metastatic squamous cell carcinoma. Response rates were 11% and 17%. No unexpected toxicities were observed.	
Todd Gersten	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The limited available data reflects activity for a small subset of patients. In those patients, the efficacy has the potential to be robust.	