COMPENDIA TRANSPARENCY TRACKING FORM

DATE: June 12, 2023

OFF-LABEL ID #: 2570

DRUG NAME: Ibrutinib

OFF-LABEL USE: Mantle cell lymphoma; In previously untreated patients, ineligible for transplant, in combination with rituximab +/- bendamustine

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	LITERATURE CODE
Monga, N, Tam, C, Garside, J, et al: Clinical efficacy and safety of first-line treatments in patients with mantle cell lymphoma: A systematic literature review. Crit Rev Oncol Hematol Feb 2021; Vol 158, p. 103212.	2
Wang, ML, Jurczak, W, Jerkeman, M, et al: Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma. N Engl J Med Jun 30, 2022; Vol 386, Issue 26; pp. 2482-2494.	S
Jain, P, Zhao, S, Lee, HJ, et al: Ibrutinib with rituximab in first-line treatment of older patients with mantle cell lymphoma. J Clin Oncol Jan 10, 2022; Vol 40, Issue 2; pp. 202-212.	S
Sheng, Z and Wang, L: Superiority of ibrutinib plus bendamustine and rituximab in newly diagnosed patients with mantle-cell lymphoma ineligible for intensive therapy: a network meta-analysis. Eur J Haematol Mar 14, 2023; Vol Epub, p. Epub.	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
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
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Ibrutinib has established efficacy in the treatment of previously untreated mantle cell lymphoma, when given in combination with rituximab, and rituximab and bendamustine (BR). A randomized trial (BR +/- ibrutinib) demonstrated an improved response rate (65% vs. 57%) but no difference in overall survival. In a single-arm phase II study, Ibrutinib + rituximab dmonstrated an overall response rate of 96% with 3y PFS of 87% and OS of 94%. Unexpected toxicity was not observed in either trial. While ibrutinib has demonstrated efficacy in this disease, its use as first line treatment may be limited to patients ineligible for other standard first line therapies.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Ibrutinib in combination with rituximab and bendamustine in untreated MCL patients demonstrated an increase in progression free survival. The studies compared Ibrutinib vs placebo. Ibrutinib might be more effective in older patients without any cardiovascular issues.	
Todd Gersten	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Ibrutinib adds efficacy to BR (improved PFS) and single agent R (improved response rate) but without overall survivorship improvement. In light of the added toxicity (increased number of grade 3/4 events and deaths in the experimental arm of the SHINE trial) I would not routinely recommend the addition of Ibrutinib to the general elderly population. The addition could be considered in a healthier elderly individual in need of a robust response rate and duration of disease control.	