IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: September 8, 2020

PACKET: 2041

DRUG: Carfilzomib

USE: Multiple myeloma; Newly diagnosed, transplant-ineligible, in combination with a chemotherapy agent and a steroid

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, 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
Mikhael,J., Ismaila,N., Cheung,M.C., et al: Treatment of multiple myeloma: ASCO and CCO joint clinical practice guideline. J Clin Oncol Apr 01, 2019; Vol Epub, p. Epub.		S
Facon T, Lee JH, Moreau P, et al. Carfilzomib or bortezomib with melphalan-prednisone for transplant-ineligible patients with newly diagnosed multiple myeloma. Blood. 2019;133(18):1953–1963.	This was an open-label, randomized phase 3 trial that compared carfilzomib- versus bortezomib-based regimens in transplant-ineligible patients with newly diagnosed multiple myeloma. The risk of potential bias associated with randomization, allocation concealment, detection, attrition, and reporting were deemed low. The open-label trial design is associated with high risk of performance bias, which was mitigated by the use of an independent review committee. Notably, there is high risk that bias could be introduced by the funder of the study collecting and analyzing all data.	S
Boccia RV, Bessudo A, Agajanian R, et al. A Multicenter, Open-Label, Phase 1b Study of Carfilzomib, Cyclophosphamide, and Dexamethasone in Newly Diagnosed Multiple Myeloma Patients (CHAMPION-2). Clin Lymphoma Myeloma Leuk. 2017;17(7):433-437.		3
Bringhen, S, D'Agostino, M, De Paoli, L, et al: Phase 1/2 Study of Weekly Carfilzomib, Cyclophosphamide, Dexamethasone in Newly Diagnosed Transplant-Ineligible Myeloma. Leukemia Apr 2018; Vol 32, Issue 4; pp. 979-985.	This study was included in the pooled analysis in Bringhen et al 2019.	S

Bringhen S, Petrucci MT, Larocca A, et al. Carfilzomib, cyclophosphamide, and dexamethasone in patients with newly diagnosed multiple myeloma: a multicenter, phase 2 study. Blood. 2014;124(1):63-69.	This study was included in the pooled analysis in Bringhen et al 2019.	S
Bringhen, S, Mina, R, Petrucci, MT, et al: Once-weekly versus twice-weekly carfilzomib in patients with newly diagnosed multiple myeloma: A pooled analysis of two phase i/ii studies. Haematologica 2019; Vol 104, Issue 8; pp. 1640-1647.	This was a pooled analysis of 2 multi-site, single-arm, phase ll studies that assessed once-weekly and twice-weekly carfilzomib combined with cyclophosphamide and dexamethasone in transplant-ineligible patients with newly diagnosed mulitple myeloma. There was low risk of bias associated with selection of cohorts and unclear risk associated with assessment of outcome. The primary efficacy endpoint was based on the intention-to-treat population, and median follow-up was 39 months (IQR, 31 to 47 months). Caveats of the study include the absence of a control group and lack of independent review of response.	S
Mina, R, Bonello, F, Petrucci, MT, et al: Carfilzomib, Cyclophosphamide and Dexamethasone for Newly Diagnosed, High-Risk Myeloma Patients Not Eligible for Transplant: A Pooled Analysis of Two Studies. Haematologica Feb 27, 2020; Vol Epub, p. Epub.		1

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
		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 IIa: Recommended, in Most Cases	The use of Carflizomib to a regimen that includes a steroid and a chemotherapy agent, shows a good overall response rate. These patients were newly diagnosed with multiple myeloma and were deemed transplant-ineligible. The adverse effects profile is something that needs to be coinsidered as they are serious and frequent.	
John Roberts	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Carfilzomib in combination with an immunomodulatory drug and a steroid has been found to be very active and acceptably safe for the treatment of newly diagnosed, transplant-ineligible myeloma. Other three drug combinations that do not include carfilzomib have show similar activity with acceptable but apparently differing toxicity profiles. There is insufficient information from comparative trials to establish guidelines regarding regimen.	

Richard LoCicero	Effective	Class IIb: Recommended, in Some Cases	Clinical trials have established the efficacy of carfilzomib, in combination with a chemotherapy agent and a steroid in the treatment of transplant-ineligible patients with newly diagnosed multiple myeloma. However, other combinations are considered more effective in this setting (i.e., bortezomib, an IMID and a steroid). Therefore, the carfilzomib regimen may be appropriate only in some cases (i.e., contraindications for other more effective regimens).	