IBM Watson Health

**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** September 3, 2020

**PACKET:** 1972

**DRUG:** Carfilzomib

**USE:** Multiple myeloma; Newly diagnosed, transplant-eligible, in combination with an immunomodulatory drug 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. | | 2 |
| Jasielec J, Kubicki T, Raje N, et al. Carfilzomib, lenalidomide, and dexamethasone plus transplant in newly diagnosed multiple myeloma [published online ahead of print, 2020 Jul 31]. Blood. 2020;blood.2020007522. | This was a multi-site, single-arm, phase ll study that assessed carfilzomib combined with lenalidomide and dexamethasone in transplant-eligible 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 56 months (range, 2.9–75.1 months). Caveats of the study include the absence of a control group and lack of independent review of response. | S |
| Sonneveld, P, Asselbergs, E, Zweegman, S, et al: Phase 2 Study of Carfilzomib, Thalidomide, and Dexamethasone as Induction/Consolidation Therapy for Newly Diagnosed Multiple Myeloma. Blood Jan 15, 2015; Vol 125, Issue 3; pp. 449-456. | This was a multi-site, single-arm, phase ll study that assessed carfilzomib combined with thalidomide and dexamethasone in transplant-eligible 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 23 months (range, 5 to 44 months). Caveats of the study include the absence of a control group and lack of independent review of response. | S |

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| Wester R, van der Holt B, Asselbergs E, et al. Phase II study of carfilzomib, thalidomide, and low-dose dexamethasone as induction and consolidation in newly diagnosed, transplant eligible patients with multiple myeloma; the Carthadex trial. Haematologica. 2019;104(11):2265-2273. | This was the follow-up to the Sonneveld 2015 publication. | S |
| Mikhael JR, Reeder CB, Libby EN, et al. Phase Ib/II trial of CYKLONE (cyclophosphamide, carfilzomib, thalidomide and dexamethasone) for newly diagnosed myeloma. Br J Haematol. 2015;169(2):219–227. | | 3 |
| Jakubowiak, AJ, Dytfeld, D, Griffith, KA, et al: A Phase 1/2 Study of Carfilzomib in Combination With Lenalidomide and Low-Dose Dexamethasone as a Frontline Treatment for Multiple Myeloma. Blood Aug 30, 2012; Vol 120, Issue 9; pp. 1801-1809. | | 3 |
| Moreau P, Kolb B, Attal M, et al. Phase 1/2 study of carfilzomib plus melphalan and prednisone in patients aged over 65 years with newly diagnosed multiple myeloma. Blood. 2015;125(20):3100-3104. | | 1 |

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|---|---|---|
| Korde, N, Roschewski, M, Zingone, A, et al: Treatment With Carfilzomib-Lenalidomide-Dexamethasone With Lenalidomide Extension in Patients With Smoldering or Newly Diagnosed Multiple Myeloma. JAMA Oncol Sep 2015; Vol 1, Issue 6; pp. 746-754. | | 3 |
| Kazandjian, D, Korde, N, Mailankody, S, et al: Remission and Progression-Free Survival in Patients With Newly Diagnosed Multiple Myeloma Treated With Carfilzomib, Lenalidomide, and Dexamethasone: Five-Year Follow-up of a Phase 2 Clinical Trial. JAMA Oncol Dec 01, 2018; Vol 4, Issue 12; pp. 1781-1783. | | 3 |
| 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. | | 2 |
| Wester, R, Zweegman, S, Van der Holt, B, et al: Eight versus four induction cycles of Carfilzomib, Thalidomide and Low-dose Dexamethasone: the Carthadex trial. Clin Lymphoma Myeloma Leukemia Oct 2019; Vol 19, Issue 10 Suppl; pp. e220-e221. | | 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 | | |
| | | John D Roberts | None |
| | | Jeffrey Klein | None |
| | | Richard LoCicero | Incyte Corporation<br><br>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 immunomodulatory agent, shows a good degree of progression free survival as well as a good overall response. These patients were newly diagnosed with multiple myeloma and were deemed transplant-eligible. The adverse effects profile is something that needs to be coinsidered as these were serious and somewhat prevalent. | |

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|---|---|---|---|---|
| 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-eligible 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 efficacy of carfilzomib in combination with IMIDs and steroids in the treatment of newly diagnosed, transplant-eligible patients. Carfilzomib is one of serveral proteosome inhibitors that are commercially available and with established efficacy. Therefore, other proteosome inhibitors may be used in this setting as well. Since bortezomib is more often used, the strength of recommendation for carfilzomib is "IIb: recommended, in Some cases." | |