**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** May 31, 2022

**OFF-LABEL ID #:** 2401

**DRUG NAME:** Bendamustine Hydrochloride

**OFF-LABEL USE:** AL amyloidosis; Relapsed or refractory, combination therapy with dexamethasone

| 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 |
|---|---|---|
| Lentzsh, S, Lagos, GG, Comenzo, RL, et al: Bendamustine with dexamethasone in relapsed/refractory systemic light-chain amyloidosis: results of a phase II study. J Clin Oncol May 01, 2020; Vol 38, Issue 13; pp. 1455-1462. | This was a prospective single-arm phase 2 clinical trial that investigated bendamustine in patients with AL amyloidosis. The risk of bias due to confounding, selection, classification of and deviation from intervention, selective reporting, and missing data were deemed low risk. The risk of bias associated with measurement of outcome was deemed moderate risk due to lack of central outcome assessment. A major caveat of the study is the lack of a control group. | S |
| Lentzsch, S, Lagos, GG, Comenzo, R, et al: Updated analysis of phase 2 study of bendamustine and dexamethasone in patients with relapsed/refractory systemic light chain (AL) amyloidosis. Amyloid 2019; Vol 26 Sup 1, pp. 113-114. | | 2 |
| Milani, P, Schonland, S, Merlini, G, et al: Treatment of AL amyloidosis with bendamustine: a study of 122 patients. Blood Nov 01, 2018; Vol 132, Issue 18; pp. 1988-1991. | | 4 |
| Milani, P, Schonland, S, Palladini, G, et al: Response to bendamustine is associated with a survival advantage in a heavily pretreated patients with AL amyloidosis. Amyloid Mar 2017; Vol 24 Sup 1, pp. 56-57. | | 4 |
| Gillmore,J.D., Wechalekar,A., Bird,J., et al: Guidelines on the diagnosis and investigation of AL amyloidosis. Br J Haematol Jan 2015; Vol 168, Issue 2; pp. 207-218. | | S |

**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<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 IIa: Recommended, in Most Cases | | B |
| Jeffrey Klein | Evidence Favors Efficacy | Class IIa: Recommended, in Most Cases | The use of Bendamustine with dexamethasone to treat relapsed or refractory AL amyloidosis appears to have good efficacy. These studies had a small number of subjects. The high percentage of adverse events in the grade 3-4 range needs to considered, as this may limit its use. | |
| Todd Gersten | Evidence Favors Efficacy | Class IIa: Recommended, in Most Cases | In a space with no standard of care options and very limited data, the combination of bendamustine/dexamethasone resulted in substantial efficacy with minimal toxicity in a single-arm phase 2 study of relapsed/refractory patients with light chain (AL) amyloidosis. This should be considered to be a very reasonable option for this patient population. | |

| | | | | |
|---|---|---|---|---|
| Richard LoCicero | Evidence Favors Efficacy | Class III: Not Recommended | A single arm phase II trial evaluated bendamustine in the treatment of relapsed or refractory AL amyloidosis. A partial hematologic response was observed in 57% of patients (16 of 28) without unexpected toxicity. Conclusions are limited by small study small and phase II design. | |