TRUVEN HEALTH ANALYTICS™

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: **December 2015**

PACKET: **1261**

DRUG: **Bortezomib**

USE: **Amyloid light chain amyloidosis**

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, R, L *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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Huang,X., et al: Induction therapy with bortezomib and dexamethasone followed by autologous stem cell transplantation versus autologous stem cell transplantation alone in the treatment of renal AL amyloidosis: A randomized controlled trial. BMC medicine Jan 06, 2014; Vol 12, Issue 1; p. 1	Comments: This was a single-center randomized controlled trial. Overall, this study was at low risk of biases associated with lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Scott,E.C., et al: Induction bortezomib in Al amyloidosis followed by high dose melphalan and autologous stem cell transplantation: a single institution retrospective study. Clin Lymphoma Myeloma Leuk. Oct 2014; Vol 14, Issue 5; pp. 424-430.		3
Gatt,M.E., et al: Outcomes of light-chain amyloidosis patients treated with first-line bortezomib: a collaborative retrospective multicenter assessment. Eur J Haematol Mar 31, 2015		3

Sanchorawala,V., et al: Induction therapy with bortezomib followed by bortezomib-high dose melphalan and stem cell transplantation for light chain amyloidosis: results of a prospective clinical trial. Biology of Blood & Marrow Transplantation Aug 2015; Vol 21, Issue 8; pp. 1445-1451		3
Palladini,G., et al: Melphalan and dexamethasone with or without bortezomib in newly diagnosed AL amyloidosis: a matched case-control study on 174 patients. Leukemia Dec 2014; Vol 28, Issue 12; pp. 2311-2316.	Comments: This was a retrospective cohort study with well-matched controls. There was low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcome. All subjects were treated at the same institution. Follow-up was a median of 26 months. All subjects were included in the analyses.	S
Venner,C.P., et al: A matched comparison of cyclophosphamide, bortezomib and dexamethasone (CVD) versus risk-adapted cyclophosphamide, thalidomide and dexamethasone (CTD) in AL amyloidosis. Leukemia Dec 2014; Vol 28, Issue 12; pp. 2304-2310.	Comments: This was a retrospective cohort study with well-matched controls. There was low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcome. All subjects were consecutively presenting unselected patients from the same institution.The median follow-up was 12.7 and 25.5 m for the CVD and CTD arms, respectively. All subjects were included in the analyses.	S
Kastritis,E., et al: Long-term outcomes of primary systemic light chain (AL) amyloidosis in patients treated upfront with bortezomib or lenalidomide and the importance of risk adapted strategies. Am J Hematol Apr 2015; Vol 90, Issue 4; pp. E60-E65.	Comments: This was a prospectove cohort study. There was low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcome. All subjects were consecutively presenting unselected patients from the same institution. The median follow-up was 57 months. Data were collected prospectively in all patients, and all were assessed and followed rigorously according to a pre-specified institutional protocol and received similar supportive care according to our institution's practice. All subjects were included in the analyses.	S

Palladini,G., et al: A European collaborative study of cyclophosphamide, bortezomib, and dexamethasone in upfront treatment of systemic AL amyloidosis. Blood Jul 30, 2015; Vol 126, Issue 5; pp. 612-615.		3
Jaccard,A., al: Efficacy of bortezomib, cyclophosphamide and dexamethasone in treatment-naive patients with high-risk cardiac AL amyloidosis (Mayo Clinic stage III). Haematologica Sep 2014; Vol 99, Issue 9; pp. 1479-1485		3
Lee,J.Y., et al: Bortezomib, melphalan, and prednisolone combination chemotherapy for newly diagnosed light chain (AL) amyloidosis. Amyloid Dec 2014; Vol 21, Issue 4; pp. 261-266.		3
Cornell,R.F., et al: Bortezomib-based induction for transplant ineligible AL amyloidosis and feasibility of later transplantation. Bone Marrow Transplant Jul 2015; Vol 50, Issue 7; pp. 914-917.		1
Landau,H., et al: Bortezomib and dexamethasone consolidation following risk-adapted melphalan and stem cell transplantation for patients with newly diagnosed light-chain amyloidosis. Leukemia Apr 2013; Vol 27, Issue 4; pp. 823-828.	Comments: This was an open-label, single-arm trial with a serious limitation. The results should be interpreted with caution since the study lacked a control group. There was possible high risk of bias with the selection of patients. There was low risk of bias associated the assessment of outcomes since they were objective and data were gathered prospectively. All subjects were included in the analyses.	S

Reece,D.E., et al: Efficacy and safety of once-weekly and twice-weekly bortezomib in patients with relapsed systemic AL amyloidosis: Results of a phase 1/2 study. Blood Jul 28, 2011; Vol 118, Issue 4; pp. 865-873.	Comments: This was an international, multi-site, open-label, single-arm, phase 1/2 trial with a serious limitation. The results should be interpreted with caution since the study lacked a control group. There was possible high risk of bias with the selection of patients. There was low risk of bias associated the assessment of outcomes since they were objective and data were gathered prospectively. Additionally, responses were confirmed by an independent data monitoring committee. All subjects were included in the analyses. Median follow-up ranged from 46 to 66 months across dose groups.	S
Reece,D.E., et al: Long-term follow-up from a phase 1/2 study of single-agent bortezomib in relapsed systemic AL amyloidosis. Blood Oct 16, 2014; Vol 124, Issue 16; pp. 2498-2506	Comments: This was an international, multi-site, open-label, single-arm, phase 1/2 trial with a serious limitation. The results should be interpreted with caution since the study lacked a control group. There was possible high risk of bias with the selection of patients. There was low risk of bias associated the assessment of outcomes since they were objective and data were gathered prospectively. Additionally, responses were confirmed by an independent data monitoring committee. All subjects were included in the analyses. Median follow-up ranged from 46 to 66 months across dose groups.	S
Venner,C.P., et al: Cyclophosphamide, bortezomib,anddexamethasone therapy in AL amyloidosis is associated with high clonal response rates and prolonged progression-free survival. Blood May 10, 2012; Vol 119, Issue 19; pp. 4387-4390.		3
Lamm,W., et al: Efficacy of the combination of bortezomib and dexamethasone in systemic AL amyloidosis. Ann Hematol Feb 2011; Vol 90, Issue 2; pp. 201-206		3

Kikukawa,Y., et al: Combined use of bortezomib, cyclophosphamide, and dexamethasone induces favorable hematological and organ responses in Japanese patients with amyloid light-chain amyloidosis: a single-institution retrospective study. Int J Hematol Feb 2015; Vol 101, Issue 2; pp. 133-139.		3
Wechalekar,A.D., Gillmore,J.D., Bird,J., et al: Guidelines on the management of AL amyloidosis. British Journal of Haematology Jan 01, 2015; Vol 168, Issue 2; pp. 186-206.		S
Weber,N., et al: Management of systemic AL amyloidosis: Recommendations of the Myeloma Foundation of Australia Medical and Scientific Advisory Group. Internal Medicine Journal Apr 2015; Vol 45, Issue 4; pp. 371-382.		S
Dispenzieri,A.: Still no certainty about the role of upfront bortezomib among patients with AL amyloidosis. Leukemia Dec 11, 2014; Vol 28, Issue 12; pp. 2273-2275.		4
Mahmood,S., et al: Update on treatment of light chain amyloidosis. Haematologica Feb 01, 2014; Vol 99, Issue 2; pp. 209-221.		4

Sanchorawala,V., et al: Bortezomib and high-dose melphalan conditioning for stem cell transplantation for AL amyloidosis: A pilot study. Haematologica Dec 01, 2011; Vol 96, Issue 12; pp. 1890-1892.		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
Felicia Gelsey, MS	None	Edward Balaban, DO	None
Stacy LaClaire, PharmD	None	Jeffrey A. Bubis, DO	None
Catherine Sabatos, PharmD	None	James E. Liebmann, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward Balaban, DO	Evidence Favors Efficacy	Class I: Recommended	With so few choices available, Bortezomib offers one of the few promising therapeutic options.	N/A
Jeffrey A. Bubis, DO	Evidence Favors Efficacy	Class IIb: Evidence Favors Efficacy	Treatment improves progression free survival and response rate, but it isn't clear that this improves overall survival, is more costly, and adds toxicity.	N/A

James E. Liebmann, MD	Effective	Class I: Recommended	Light chain amyloidosis (AL) is a rare condition due to a plasma cell neoplasm. Treatment of this disorder has been based on myeloma treatment for over forty years. There are very few randomized trials of therapy for AL (Huang et al is one of the few). The papers submitted for review confirm that bortezomib is a very active drug in the treatment of AL. It is generally well tolerated, particularly in patients with cardiac dysfunction. It should, however, be used with caution, if used at all, in patients with severe peripheral neuropathy from AL. With the exception of patients with severe neuropathy, bortezomib should be considered a standard drug for treatment of AL.	N/A