IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 12/13/2019

PACKET: 1942

DRUG: Lenalidomide

USE: AL amyloidosis; Relapsed or refractory, combination therapy

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	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Mahmood,S., Venner,C.P., Sachchithanantham,S., et al: Lenalidomide and dexamethasone for systemic AL amyloidosis following prior treatment with thalidomide or bortezomib regimens. British Journal of Haematology Sep 2014; Vol 166, Issue 6; pp. 842-848.	This was a retrospective cohort study that assessed lenalidomide and dexamethasone treatment in patients with relapsed/refractory light chain amyloidosis. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for outcomes, and all identified subjects were included in the primary analyses. One caveat of the study is that it lacked a control group.	3
Hegenbart, U, Bochtler, T, Benner, A, et al: Lenalidomide/ melphalan/ dexamethasone in newly diagnosed patients with immunoglobulin light chain amyloidosis: results of a prospective phase 2 study with long-term follow up. Haematologica Aug 2017; Vol 102, Issue 8; pp. 1424-1431.		1
Kumar, SK, Hayman, SR, Buadi, FK, et al: Lenalidomide, cyclophosphamide, and dexamethasone (CRd) for light-chain amyloidosis: long-term results from a phase 2 trial. Blood May 24, 2012; Vol 119, Issue 21; pp. 4860-4867.		1
Sanchorawala, V, Wright, DG, Rosenzweig, M, et al: Lenalidomide and dexamethasone in the treatment of AL amyloidosis: results of a phase 2 trial. Blood Jan 15, 2007; Vol 109, Issue 2; pp. 492-496.	This was a phase 2 clinical trial that assessed lenalidomide with or without dexamethasone treatment in patients with light chain amyloidosis. There was low risk of bias associated with selection of cohorts and high risk of bias for assessment of outcomes. Data was gathered prospectively for outcomes. The attrition rate was high, with 29% of subjects withdrawing from the study. Another caveat of the study is that it lacked a control group.	3

Cibeira, MT, Oriol, A, Lahuerta, JJ, et al: A phase II trial of lenalidomide, dexamethasone and cyclophosphamide for newly diagnosed patients with systemic immunoglobulin light chain amyloidosis. Br J Haematol Sep 2015; Vol 170, Issue 6; pp. 804-813.		1
Palladini, G, Russo, P, Foli, A, et al: Salvage therapy with lenalidomide and dexamethasone in patients with advanced AL amyloidosis refractory to melphalan, bortezomib, and thalidomide. Ann Hematol Jan 2012; Vol 91, Issue 1; pp. 89-92.	This was an open-label, single-arm phase II clinical trial that assessed lenalidomide and dexamethasone treatment in patients with refractory light chain amyloidosis. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes, and all subjects were included in the analyses. One caveat of the study is that it lacked a control group.	S
Dispenzieri, A, Lacy, MQ, Zeldenrust, SR, et al: The activity of lenalidomide with or without dexamethasone in patients with primary systemic amyloidosis. Blood Jan 15, 2007; Vol 109, Issue 2; pp. 465-470.		1
Palladini,G., Russo,P., Milani,P., et al: A phase II trial of cyclophosphamide, lenalidomide and dexamethasone in previously treated patients with AL amyloidosis. Haematologica Mar 2013; Vol 98, Issue 3; pp. 433-436.	This was an open-label, single-arm phase II clinical trial that assessed cyclophosphamide, lenalidomide, and dexamethasone treatment in patients with relapsed/refractory light chain amyloidosis. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes, and all subjects were included in the analyses. One caveat of the study is that it lacked a control group.	S
Sanchorawala, V, Patel, JM, Sloan, JM, et al: Melphalan, lenalidomide and dexamethasone for the treatment of immunoglobulin light chain amyloidosis: results of a phase II trial. Haematologica May 2013; Vol 98, Issue 5; pp. 789-792.		1

Kastritis, E, Terpos, E, Roussou, M, et al: A phase 1/2 study of lenalidomide with low-dose oral cyclophosphamide and low-dose dexamethasone (RdC) in AL amyloidosis. Blood Jun 07, 2012; Vol 119, Issue 23; pp. 5384-5390.		1
Moreau P, Jaccard A, Benboubker L, et al: Lenalidomide in combination with melphalan and dexamethasone in patients with newly diagnosed AL amyloidosis: a multicenter phase 1/2 dose-escalation study. Blood Dec 02, 2010; Vol 116, Issue 23; pp. 4777-4782.		1
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

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
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Two single arm studies evaluated the use of lenalidomide in the treatment of relapsed/refractory AL amyloidosis. Hematologic response rates were 62% (in combination with cyclophosphamide and dexamethasone) and 41% (in combination with dexamethasone). Further conclusions are limited by the absence of comparator arms. Unexpected toxicity was not observed.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of Lenalidomide in combination with 1 or 2 other agents shows a good overall response. The incidence of adverses effects with some being serious has to be taken into consideration. Theses studies were generally quite small as well.	
John Roberts	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Two phase 2 studies of lenolidamide in combination with either dexamethasone or dexamethasone/cyclophosphamide in previously treated patients showed moderate toxicity with frequent dose reductions and promising results in terms of response rates. There are many treatment options for amyloidosis, and few comparative trials upon which to base treatment decisions.	