IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 11/03/2020

PACKET: 2034

DRUG: Daratumumab

USE: AL amyloidosis - Relapsed or refractory

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: A, C, L, R *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
Wechalekar AD, Gillmore JD, Bird J, et al. Guidelines on the management of AL amyloidosis. Br J Haematol. 2015;168(2):186-206.		S
O'Meara, E, McDonald, M, Chan, M, et al: CCS/CHFS Heart Failure Guidelines: Clinical Trial Update on Functional Mitral Regurgitation, SGLT2 Inhibitors, ARNI in HFpEF, and Tafamidis in Amyloidosis. Can J Cardiol Feb 2020; Vol 36, Issue 2; pp. 159-169.		2
Kimmich CR, Terzer T, Benner A, et al. Daratumumab for systemic AL amyloidosis: prognostic factors and adverse outcome with nephrotic-range albuminuria. Blood. 2020 Apr 30;135(18):1517-1530.	This study was a review of consecutive patients with previously-treated light chain amyloidosis who were treated with either daratumumab/dexamethasone or daratumumab/bortezomib/dexamethasone. The risk of bias associated with selection of participants, classification of intervention, deviation from intervention, missing data, measurement of outcome, and reporting bias were deemed low risk. The risk of bias associated with confounders was deemed high risk.	S
Chung, A, Kaufman, GP, Sidana, S, et al: Organ responses with daratumumab therapy in previously treated AL amyloidosis. Blood Adv Feb 11, 2020; Vol 4, Issue 3; pp. 458-466.	This study was a retrospective review of medical records that investigated treatment with daratumumab monotherapy in patients with previously treated light chain amyloidosis. The risk of bias due to unmeasured confounders and missing data were deemed high risk. The risk of bias associated with selection, classification of intervention, deviation from intervention, measurement of outcome, and reporting bias were deemed low risk. Data was collected retrospectively from medical records. One caveat of the study is the lack of a control group.	S

Milani P, Fazio F, Basset M, et al. High rate of profound clonal and renal responses with daratumumab treatment in heavily pre-treated patients with light chain (AL) amyloidosis and high bone marrow plasma cell infiltrate. Am J Hematol. 2020 Aug;95(8):900-905.		1
Cohen, OC, Brodermann, MH, Blakeney, IJ, et al: Rapid response to single agent daratumumab is associated with improved progression-free survival in relapsed/refractory AL amyloidosis. Amyloid Sep 2020; Vol 27, Issue 3; pp. 200-205.		2
Roussel, M, Merlini, G, Chevret, S, et al: A prospective phase 2 trial of daratumumab in patients with previously treated systemic light-chain amyloidosis. Blood Apr 30, 2020; Vol 135, Issue 18; pp. 1531-1540.	This study was a phase 2 single-arm trial that assessed daratumumab therapy in patients with previously-treated light chain amyloidosis. All risk of bias domains - unmeasured confounders, selection of participants, classification of intervention, deviation from intervention, missing data, measurement of outcome, and reporting bias - were deemed low risk. One caveat of the study is the lack of a control group.	S
Lecumberri, R, Krsnik, I, Askari, E, et al: Treatment with daratumumab in patients with relapsed/refractory AL amyloidosis: a multicentric retrospective study and review of the literature. Amyloid Sep 2020; Vol 27, Issue 3; pp. 163-167.		3

Kaufman,G.P., Schrier,S.L., Lafayette,R.A., et al: Daratumumab yields rapid and deep hematologic responses in patients with heavily pretreated AL amyloidosis. Blood Aug 17, 2017; Vol 130, Issue 7; pp. 900-902.	See comments for Chung et al 2020	S
Sanchorawala, V, Sarosiek, S, Schulman, A, et al: Safety, tolerability, and response rates of daratumumab in relapsed AL amyloidosis: results of a phase 2 study. Blood Apr 30, 2020; Vol 135, Issue 18; pp. 1541-1547.		3
Khouri, J, Kin, A, Thapa, B, et al: Daratumumab proves safe and highly effective in AL amyloidosis. Br J Haematol Apr 2019; Vol 185, Issue 2; pp. 342-344.		3
Milani, P, Basset, M, Curci, P, et al: Daratumumab in light chain deposition disease: rapid and profound hematologic response preserves kidney function. Blood Adv Apr 14, 2020; Vol 4, Issue 7; pp. 1321-1324.		1
Basset, M, Nuvolone, M, Palladini, G, et al: Novel challenges in the management of immunoglobulin light chain amyloidosis: from the bench to the bedside. Expert Rev Hematol Aug 11, 2020; Vol Epub, p. Epub.		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 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 Daratumumab in previously treated AL amyloidosis patients in generally small studies appears to be effective and most patients achieved a good organ response. Adverse effects were mild and minimal. It remains to be seen whether the response would be even better if chemotherapy were added to the regimen.	

John Roberts	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	One prospective and several retrospective single arm trials show response in likely clinically meaningful parameters with daratumumab treatment in relapsed/refractory AL amyloidosis. All patients received at least one dose of dexamethasone, and most received prolonged dexamethasone and/or other agents. Treatment was well tolerated with minor infusion reactions. Most other observed adverse events likely were due to the underlying disease, not the treatment. It remains possible, albeit unlikely, that appropriately controlled studies would reveal important disadvantages.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	At least four phase II trials have established the efficacy of daratumumab for the treatment of relapsed or refractory AL amyloidosis without unexpected toxicity. The absence of randomized phase III trials limits the strength of the recommendation.	