IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 8/7/2019

PACKET: 1877

DRUG: Cladribine

USE: Acute myeloid leukemia, disease; Induction 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, E, 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
Zhou A, Han Q, Song H, et al. Efficacy and toxicity of cladribine for the treatment of refractory acute myeloid leukemia: a meta-analysis. Drug Des Devel Ther. 2019 May 29;13:1867-1878.	This was a systematic review and meta-analysis that included ten prospective cohort trials in 422 patients with refractory AML receiving cladribine monotherapy or combination therapy. The systematic review authors conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The authors used the Newcastle-Ottawa Scale to assess the quality of the included trials. They also found evidence of publication bias in terms of the primary outcomes. The primary analyses showed high heterogeneity (I2 > 75%), and the authors conducted subgroup analyses to explore this heterogeneity. This meta-analysis provides a summary of the available literature in the paucity of randomized-controlled trials.	S
Holowiecki,J., Grosicki,S., Giebel,S., et al: Cladribine, but not fludarabine, added to daunorubicin and cytarabine during induction prolongs survival of patients with acute myeloid leukemia: a multicenter, randomized phase III study. J.Clin Oncol. Jul 10, 2012; Vol 30, Issue 20; pp. 2441-2448.	This was an open-label, multi-centre, randomized-controlled phase III trial that assessed three induction therapy regimens (DA, DA + Cladribine, and DA + Fludarabine) in patients with acute myeloid leukemia (AML). The risk of potential bias associated with randomization, attrition, and reporting were deemed low. The risk of potential bias associated with allocation concealment, performance, and detection were deemed high due to the open-label study design.	S
Pluta,A., Robak,T., Wrzesien-Kus,A., et al: Addition of cladribine to the standard induction treatment improves outcomes in a subset of elderly acute myeloid leukemia patients. Results of a randomized Polish Adult Leukemia Group (PALG) phase II trial. Am.J.Hematol. Apr 2017; Vol 92, Issue 4; pp. 359-366.	This was an open-label, multi-centre, randomized-controlled phase II trial that assessed Cladribine addition to standard induction therapy in patients with acute myeloid leukemia (AML). The risk of potential bias associated with randomization, attrition, and reporting were deemed low. The risk of potential bias associated with allocation concealment, performance, and detection were deemed high due to the open-label study design.	S

Holowiecki J, Grosicki S, Robak T, et al. Addition of cladribine to daunorubicin and cytarabine increases complete remission rate after a single course of induction treatment in acute myeloid leukemia. Multicenter, phase III study. Leukemia. 2004 May;18(5):989-97.		2
Park,H., Youk,J., Kim,I., et al: Comparison of cladribine- and fludarabine-based induction chemotherapy in relapsed or refractory acute myeloid leukaemia. Ann Hematol Oct 2016; Vol 95, Issue 11; pp. 1777-1786.		2
Bao,Y., Zhao,J., and Li,Z.Z.: Comparison of clinical remission and survival between CLAG and FLAG induction chemotherapy in patients with refractory or relapsed acute myeloid leukemia: a prospective cohort study. Clin Transl.Oncol. Jul 2018; Vol 20, Issue 7; pp. 870-880.		2
Muluneh, Benyam et al. A Comparison of Clofarabine-based (GCLAC) and Cladribine-based (CLAG) Salvage Chemotherapy for Relapsed/Refractory AML. Clinical Lymphoma, Myeloma and Leukemia. Jan 2018; Vol 18, Issue 1; e13 - e18.		2

Xu,J., Lv,T.T., Zhou,X.F., et al: Efficacy of common salvage chemotherapy regimens in patients with refractory or relapsed acute myeloid leukemia: A retrospective cohort study. Medicine.(Baltimore.) Sep 2018; Vol 97, Issue 39; p. e12102.		2

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		
Margi Schiefelbein, PA	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
John Roberts	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	In a single multicenter randomized trial, addition of cladribine to a standard duanorubicin/cytosine arabinoside induction regimen improved overall survival in adults 17 to 60 years with acute myelogenous leukemia. A retrospective analysis of a previous multicenter randomized trial limited to adults 60 years and older showed similar results in the 60-65 year age group but no benefit in persons > 65 years.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The addition of cladribine in induction therapy for AML has been shown to improve some clinical outcomes as evaluated in a meta-analysis and 2 randomized trials. Subset analysis limits generalization of conclusions.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of cladribine as a combination therapy in AML induction patients is quite effective. Increased overall survival was demonstrated. The response for patients over the age of 65 was not as beneficial however. The degree of adverse effects was moderate.	