TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: July 2015

PACKET: 1236

DRUG: Alemtuzumab

INDICATION: Chronic lymphocytic leukemia

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, 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)]

TRUVEN HEALTH ANALYTICS

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Skoetz,N., Bauer,K., Elter,T., et al: Alemtuzumab for patients with chronic lymphocytic leukaemia. Cochrane Database Syst Rev 2012; Vol 2, p. CD008078.	This was a Cochrane systematic review that included five randomized-controlled trials which included a total of 845 patients. The risk of bias tool was used to assess the quality of the included trials. Overall, the studies were of moderate quality. Two trials were stopped prematurely due to an increased incidence of severe infections or an increase in mortality in the alemtuzumab arm. All of the criteria of the SR/MA worksheet were fulfilled.	S
Geisler,C.H., van,T.',V, Jurlander,J., et al: Frontline low-dose alemtuzumab with fludarabine and cyclophosphamide prolongs progression-free survival in high-risk CLL. Blood May 22, 2014; Vol 123, Issue 21; pp. 3255-3262.	This was an open-label randomized trial. Overall, this study was at low risk for most of the key risk of bias criteria which included 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
Elter,T., Gercheva-Kyuchukova,L., Pylylpenko,H., et al: Fludarabine plus alemtuzumab versus fludarabine alone in patients with previously treated chronic lymphocytic leukaemia: a randomised phase 3 trial. lancet oncology Dec 2011; Vol 12, Issue 13; pp. 1204-1213.	This study is included in the Cochrane 2012 systematic review by Skoetz et al.	2

Lepretre,S., Aurran,T., Mahe,B., et al: Excess mortality after treatment with fludarabine and cyclophosphamide in combination with alemtuzumab in previously untreated patients with chronic lymphocytic leukemia in a randomized phase 3 trial. Blood May 31, 2012; Vol 119, Issue 22; pp. 5104-5110.	This study is included in the Cochrane 2012 systematic review by Skoetz et al.	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
Margi Schiefelbein, PA	None	Edward Balaban, DO	None
Stacy LaClaire, PharmD	None	Jeffrey Patton, MD	None
Felicia Gelsey, MS	None	James E. Liebmann, MD	None
		Jeffrey A. Bubis, DO	None
		Keith Thompson, 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 IIb: Recommended in Some Cases	Alemtuzumab is approved for CLL. It has fair efficacy, but also has propensity to provoke corollary infections.	N/A
Jeffrey Patton, MD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	None	N/A

James E. Liebmann, MD	Effective	Class IIb: Recommended in Some Cases	This is a very odd circumstance to review. That alemtuzumab is effective in CLL is not in question. It was approved by the FDA in 2001 for the treatment of CLL in patients who relapsed after fludarabine treatment. The Geisler study included in this review was a trial of alemtuzumab as initial treatment of CLL. While their results, not suprsisingly, show that alemtuzumab increases response and (possibly) survival when given with oral fludarabine and oral cyclophosphamide, it is not clear to me that this would be a standard regimen in the US; nor is it clear that this would be superior to fludarabine and Cytoxan (given via any route) together with ritiuximab. The Cochrane review summarizes the data that led to the original approval of alemtuzumab over a decade ago. Alemtuzumab is active in this disease, but it should probably be restricted to patients with recurrent CLL. Given the introduction of ibrutinib and idelalisib, it is not at all clear to me where alemtuzumab should be used – perhaps only as a last resort in medically fit patients.	N/A
Jeffrey A. Bubis, DO	Evidence Favors Efficacy	Class IIb: Recommended in Some Cases	Although evidence favors efficacy, this comes at a significant riske of infection. Consideration of risk:benefit ratio is needed for appropriate patient selection.	N/A
Keith Thompson, MD	Evidence Favors Efficacy	Class IIb: Recommended in Some Cases	None	N/A

TRUVEN
HEALTH ANALYTICS