TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Alemtuzumab

INDICATION: Primary cutaneous T-cell lymphoma, 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**
*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
Querfeld,C., et al: Alemtuzumab for relapsed and refractory erythrodermic cutaneous T-cell lymphoma: a single institution experience from the Robert H. Lurie Comprehensive Cancer Center. Leuk Lymphoma Dec 2009; Vol 50, Issue 12; pp. 1969-1976.	Study methodology comments: This was an open-label time-series trial that should be interpreted with caution. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. This study lacked: 1) a power analysis; 2) blinding of investigators or use of independent assessors; and 3) control for other possible confounding factors. Other weaknesses were 1) selection bias may have been present since the patients were not recruited randomly or sequentially and 2) small sample size. Strengths of the study were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined clinical response; 3) presented 95% confidence intervals; 4) confirmed complete response at 4 weeks; and 5) had both inclusion and exclusion criteria.	S
Lundin,J.: Phase 2 study of alemtuzumab (anti-CD52 monoclonal antibody) in patients with advanced mycosis fungoides/Sezary syndrome. Blood Jun 01, 2003; Vol 101, Issue 11; pp. 4267-4272.	Study methodology comments: This was an open-label time-series trial that should be interpreted with caution. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. This study lacked: 1) a power analysis; 2) blinding of investigators or use of independent assessors; 3) confidence intervals; and 4) control for other possible confounding factors. Other weaknesses were 1) selection bias may have been present since the patients were not recruited randomly or sequentially and 2) small sample size. Strengths of the study were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary outcomes and clinical response; 3) confirmed diagnosis; 4) stratified response by disease site; and 5) had both inclusion and exclusion criteria.	S
Bernengo, M.G., et al: Low-dose intermittent alemtuzumab in the treatment of Sezary syndrome: clinical and immunologic findings in 14 patients. Haematologica Jun 2007; Vol 92, Issue 6; pp. 784-794.	Study methodology comments: This was an open-label time-series trial that should be interpreted with caution. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. This study lacked: 1) a power analysis; 2) blinding of investigators or use of independent assessors; and 3) control for other possible confounding factors. Other weaknesses were 1) selection bias may have been present since the patients were not recruited randomly or sequentially and 2) small sample size. Strengths of the study were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined clinical response; 3) presented 95% confidence intervals visually for some outcomes; and 4) had both inclusion and exclusion criteria.	S

Kennedy,G.A., et al: Treatment of patients with advanced mycosis fungoides and Sezary syndrome with alemtuzumab. European Journal of Haematology Oct 2003; Vol 71, Issue 4; pp. 250-256.		3
Alinari,L.: Subcutaneous alemtuzumab for Sezary Syndrome in the very elderly. Leukemia Research Aug 01, 2008; Vol 32, Issue 8; pp. 1299-1303.		3
Capalbo,S.: Mycosis Fungoides/Sezary Syndrome: A Report of Three Cases Treated with Campath-1H as Salvage Treatment. Medical Oncology Dec 01, 2003; Vol 20, Issue 4; pp. 389-396.		3
Weder,P., et al: Familial cutaneous mycosis fungoides: successful treatment with a combination of gemcitabine and alemtuzumab. Dermatology (Basel, Switzerland) 2004; Vol 208, Issue 3; pp. 281-283.		3
Gutierrez, A., et al: Treatment with alemtuzumab in a case of refractory primary cutaneous CD30-negative CD8-positive cytotoxic large T-cell lymphoma. European Journal of Haematology May 2004; Vol 72, Issue 5; pp. 377-378.		3
Gautschi,O., et al: Successful treatment of chemotherapy-refractory Sezary syndrome with alemtuzumab (Campath-1H). European Journal of Haematology Jan 2004; Vol 72, Issue 1; pp. 61-63.		3

Goteri,G., et al: Severe diarrhoea during Campath-1H treatment for refractory cutaneous T-cell lymphoma. Annals of Hematology Sep 2006; Vol 85, Issue 9; pp. 617-619.		3
Gibbs, S.D.J., et al: Alemtuzumab: effective monotherapy for simultaneous B-cell chronic lymphocytic leukaemia and Sezary syndrome. European Journal of Haematology Dec 2004; Vol 73, Issue 6; pp. 447-449.		3
Ure,U.B., et al: Alemtuzumab in Sezary syndrome: efficient but not innocent. European Journal of Dermatology - EJD Nov 2007; Vol 17, Issue 6; pp. 525-529.		3
Ravandi,F., et al: Phase II study of alemtuzumab in combination with pentostatin in patients with T-cell neoplasms. J Clin Oncol Nov 10, 2009; Vol 27, Issue 32; pp. 5425-5430.		3
Hagberg,H., et al: Phase II study of alemtuzumab (Campath-1H) in patients with advanced mycosis fungoides Sezary syndrome. Blood Nov 16, 2001; Vol 98, Issue 11 Part 1; p. 806a.		3
Gibbs,S.D., et al: Prolonged severe pancytopenia and myelodysplastic features following alemtuzumab therapy in patients with cutaneous T-cell lymphomas. Blood Nov 16, 2004; Vol 104, Issue N11,1; pp. 723A-724A.		3

Zinzani,P.L., et al: Phase II study of alemtuzumab treatment in patients with pretreated T-cell lymphoma. Blood Nov 16, 2004; Vol 104, Issue N11,2; pp. 235B-235B.		3
Porcu,P., et al: Phase I trial of subcutaneous (SQ) alemtuzumab (A) and CHOP in T-cell lymphoma: Preliminary results. Journal of Clinical Oncology Jun 20, 2006; Vol 24, Issue N18,1,S; pp. 445S-445S.		3
Beltran-Garate,B., et al: Alemtuzumab in patients with advanced mycosis fungoides and Sezary syndrome. Blood Nov 16, 2007; Vol 110, Issue 11, Part 1; pp. 1003A-1004A.		3
Beltran-Garate,B., et al: Alemtuzumab in patients with advanced mycosis fungoids: First interim report. Blood Nov 16, 2006; Vol 108, Issue 11, Part 2; pp. 264B-265B.		3
Rupoli, S., et al. Alemtuzumab in Combination with Interferon- or Gemcitabine in Aggressive and Advanced Cutaneous T-Cell Lymphomas: Report of Preliminary Results. ASH abstract 2008.		3
Fisher, D.C., et al. Low-Dose Alemtuzumab Is Uniquely Effective in Refractory Leukemic Cutaneous T Cell Lymphoma (L-CTCL). ASH abstract 2009.		3
Beltran-Garate, B., et al. Alemtuzumab in Patients with Advanced Mycosis Fungoides and Sezary Syndrome. ASH 2007 abstract.		3

Poire,X., et al: Alemtuzumab and modified capizzi regimen for the treatment of refractory enteropathy associated T-cell lymphoma. Acta Clinica Belgica Aug 2007; Vol 62, Issue N4; pp. 260-260.		3
Faguer,S., et al: Acute cutaneous T-cell lymphoma transformation during treatment with alemtuzumab. British Journal of Dermatology Oct 2007; Vol 157, Issue 4; pp. 841-842.		4
Zinzani,P.,et al: Preliminary observations of a phase II study of reduced-dose alemtuzumab treatment in patients with pretreated T-cell lymphoma. Haematologica May 2005; Vol 90, Issue 5; pp. 702-703.		4
Gardner,J.M.: Update on treatment of cutaneous T-cell lymphoma. Current Opinion in Oncology Mar 01, 2009; Vol 21, Issue 2; pp. 131-137.		4
Duvic,M: Systemic monotherapy vs combination therapy for CTCL: rationale and future strategies. Oncology (Williston Park, N Y) Feb 2007; Vol 21, Issue 2 Suppl 1; pp. 33-40.		4
Gribben,J.G.: Rediscovering alemtuzumab: Current and emerging therapeutic roles. British Journal of Haematology Mar 01, 2009; Vol 144, Issue 6; pp. 818-831.		4
Trautinger,F.: EORTC consensus recommendations for the treatment of mycosis fungoides/Sezary syndrome. European Journal of Cancer May 01, 2006; Vol 42, Issue 8; pp. 1014-1030.		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)

TRUVEN HEALTH ANALYTICS

CONTRIBUTORS:
*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Amy Hemstreet, PharmD	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffrey F. Patton, MD	None
		Keith A. Thompson, MD	None
		John M. Valgus, PharmD	None

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---		Discussed indication. Decided to use general cutaneous T-cell lymphoma. Most information pertained to SS and MF., most common forms of primary CTLC. Decided to summarize both Lundin et al. and Querfeld, et al trials, as literature is scarce and small studies. Used Bernengo trial for summary only, as unique dosing strategy	B
Edward P. Balaban, DO	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	Looks promising! Will need to see more data-studies; suspect a multi-institutional study will need to be done if possible with otherwise (….) rare disease. .	N/A

James E. Liebmann, MD	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	Although only 55 patients are presented, the overall response of MF/SS to Alemtuzumab (73%) is impressive and consistent across the three studies. This is a rationale drug to use in selected cases of MF/SS. Given the immune suppression and infection risk associated with the drug, its use should be limited to selected patients with recurrent disease.	N/A
Jeffrey F. Patton, MD	Evidence Favors Efficacy	Class IIa Recommended, In Most Cases	None	N/A
Keith A. Thompson, MD	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	None	N/A
John M. Valgus, PharmD	Effective	Class IIa Recommended, In Most Cases	All evidence suggests this agent is effective for T-Cell cut(aneous) lymphoma. However, the evidence is limited by small numbers and lack of randomization.	N/A