TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Antithymocyte globulin equine

INDICATION: Myelodysplastic syndrome

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, 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
Passweg,J.R., et al: Immunosuppressive therapy for patients with myelodysplastic syndrome: a prospective randomized multicenter phase III trial comparing antithymocyte globulin plus cyclosporine with best supportive care--SAKK 33/99. J Clin Oncol Jan 20, 2011; Vol 29, Issue 3; pp. 303-309.	Study methodology comments: This was an open-label, randomized-controlled trial. Overall, this study was at low risk for all key criteria which included lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. Allocation concealment was unclear and not discussed in the paper. The study stratified patients according to center and IPSS risk score. Data on the primary endpoint was collected before patients were permitted to cross over from BSC to ATG+CSA. The study was not powered to detect a difference between groups in survival.	S
Molldrem,J.J., et al: Antithymocyte globulin for treatment of the bone marrow failure associated with myelodysplastic syndromes. Annals of Internal Medicine Aug 06, 2002; Vol 137, Issue 3; pp. 156-163.	Study methodology comments: This was a prospective single-arm trial. There was low risk of bias associated with selection of cohorts and assessment of outcome. All subjects were included in the analyses. Statistical analyses were conducted to assess the effect of study entry characteristics and response on survival and disease progression. A major caveat of the study was the absence of a control group or active comparator.	S
Stadler,M., et al: A prospective, randomised, phase II study of horse antithymocyte globulin vs rabbit antithymocyte globulin as immune-modulating therapy in patients with low-risk myelodysplastic syndromes. Leukemia Mar 2004; Vol 18, Issue 3; pp. 460-465.		3
Molldrem,J.J., et al: Antithymocyte globulin for patients with myelodysplastic syndrome. Br J Haematol Dec 1997; Vol 99, Issue 3; pp. 699-705.		2

Kadia,T.M., et al: Final results of the phase II study of rabbit anti-thymocyte globulin, ciclosporin, methylprednisone, and granulocyte colony-stimulating factor in patients with aplastic anaemia and myelodysplastic syndrome. British Journal of Haematology May 2012; Vol 157, Issue 3; pp. 312-320		3
Sloand,E.M., et al: Factors affecting response and survival in patients with myelodysplasia treated with immunosuppressive therapy. Journal of Clinical Oncology May 20, 2008; Vol 26, Issue 15; pp. 2505-2511.		3
Yazji,S., et al: Antithymocyte globulin (ATG)-based therapy in patients with myelodysplastic syndromes. Leukemia Nov 2003; Vol 17, Issue 11; pp. 2101-2106.		3
Scott,B.L., et al: Anti-thymocyte globulin plus etanercept as therapy for myelodysplastic syndromes (MDS): a phase II study. Br J Haematol Jun 2010; Vol 149, Issue 5; pp. 706-710.		3
Broliden,P.A., et al: Antithymocyte globulin and cyclosporine A as combination therapy for low-risk non-sideroblastic myelodysplastic syndromes. Haematologica May 2006; Vol 91, Issue 5; pp. 667-670.		3
Nachtkamp,K., et al: Impact on survival of different treatments for myelodysplastic syndromes (MDS). Leuk Res Jan 29, 2009; p. 1.		3

Garg,R., et al: Phase II study of rabbit anti-thymocyte globulin, cyclosporine and granulocyte colony-stimulating factor in patients with aplastic anemia and myelodysplastic syndrome. Leukemia Jul 2009; Vol 23, Issue 7; pp. 1297-1302.		3
Deeg,H.J., et al: Hematologic responses of patients with MDS to antithymocyte globulin plus etanercept correlate with improved flow scores of marrow cells. Leuk Res Nov 2004; Vol 28, Issue 11; pp. 1177-1180.		3
Steensma,D.P., et al: Antithymocyte globulin has limited efficacy and substantial toxicity in unselected anemic patients with myelodysplastic syndrome. Blood Mar 15, 2003; Vol 101, Issue 6; pp. 2156-2158.		3
Martin,M.G., et al: Allo-SCT conditioning for myelodysplastic syndrome and acute myeloid leukemia with clofarabine, cytarabine and ATG. Bone Marrow Transplant Jan 12, 2009; p. 1.		3
Risitano,A.M.: Immunosuppressive therapies in the management of acquired immune-mediated marrow failures. Current Opinion in Hematology Jan 2012; Vol 19, Issue 1; pp. 3-13.		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
Margi Schiefelbein, PA	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Keith A. Thompson, MD	None
		Gerald J. Robbins, MD	None
		Jeffrey F. Patton, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward P. Balaban, DO	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	Although mildly efficacious, immunosuppressive therapy success Seems mostly related to the 'hypoplastic' myelodysplastic. Appears efficacious, but needs more supportive data.	N/A

James E. Liebmann, MD	Evidence is inconclusive	Class III - Not Recommended	While both the phase ll trial from Neal Young's group and the phase lll SAKK trial show similar response rates with ATG in this population, there is no evidence of an effect on survival or resource utilization with ATG. Further, these studies were conducted before there was more wide spread use of hypomethylating agents and lenalidomide. Both studies showed best response in young patients with hypoplastic disease of short duration – these patients would most likely be offered an approved drug or transplant today. Certainly the current limited data do not justify use of ATG in the vast majority of patients with MDS.	N/A
Keith A. Thompson, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	May be useful to reduce transfusions.	N/A
Gerald J. Robbins, MD	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	This disease is noted for low responses except with newer hypomethylating agents. There have been several phase 2 trials in addition to those included with relatively consistent response rate. Patients who have certain characteristics have better response rates. Clearly there are some patients with MDS who will benefit. The phase lll trial has multiple limitations, but response rates for treated patients are on par with prior studies and better than BSC. More research is needed to better define class of patients who will respond, but agent should be available in selected cases. Please also see excellent review in Seminars in hematology, Volume 49, No. 4, October 2012; pages 304-312.	N/A

Jeffrey F. Patton, MD	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	None	N/A