TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Rituximab

INDICATION: Post-transplant lymphoproliferative disorder [pediatric patients]

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, L, P, 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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Gupta,S., et al: Post-transplant lymphoproliferative disorder in children: Recent outcomes and response to dual rituximab/low-dose chemotherapy combination. Pediatric Transplantation Nov 2010; Vol 14, Issue 7; pp. 896-902.	Study methodology comments: This was an open-label, retrospective cohort study. The results should be interpreted with much caution since the study was not powered and the different treatment groups were very small (ranged from 4 to 8 patients). Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) no inclusion or exclusion criteria; and 3) did not control for the effect of potential confounding factors on outcomes. Strengths were 1) defined response and 2) reduced possible selection bias by recruiting from all presenting patients.	S
Gallego,S., et al: Post-transplant lymphoproliferative disorders in children: The role of chemotherapy in the era of rituximab. Pediatric Transplantation Feb 2010; Vol 14, Issue 1; pp. 61-66	Study methodology comments: This was an open-label, cohort study. The results should be interpreted with much caution since the study was not powered and the treatment groups were very small. Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) no inclusion or exclusion criteria; and 3) did not control for the effect of potential confounding factors on outcomes. Strengths were 1) had a control group; 2) defined response; and 3) reduced possible selection bias by recruiting from all presenting patients.	S
Faye,A., et al: Chimaeric anti-CD20 monoclonal antibody (rituximab) in post-transplant B-lymphoproliferative disorder following stem cell transplantation in children. British Journal of Haematology 2001; Vol 115, Issue 1; pp. 112-118.	Study methodology comments: This was an open-label, retrospective cohort study that should be interpreted with much caution. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) absence of power analysis; 3) no inclusion or exclusion criteria; 4) did not examine the effect of potential confounding factors on outcomes; and 5) small sample size. Strengths were 1) defined response and 2) reduced possible selection bias since all patients were recruited.	S
Wilsdorf,N., et al: EBV-specific T cell immunity in pediatric solid organ graft recipients with lymphoproliferative disease. Transfusion Medicine and Hemotherapy 2011; Vol 38 SUPPL. 1, p. 52.		2

Tsirigotis,P., et al: Post-autologous stem cell transplantation administration of rituximab improves the outcome of patients with aggressive B cell non-Hodgkin's lymphoma. Annals of Hematology Mar 2010; Vol 89, Issue 3; pp. 263-272.		1
Messahel,B., et al: Single agent efficacy of rituximab in childhood immunosuppression related lymphoproliferative disease: A United Kingdom Children's Cancer Study Group (UKCCSG) retrospective review. Leukemia and Lymphoma Dec 2006; Vol 47, Issue 12; pp. 2584-2589.	Study methodology comments: This was an open-label, retrospective cohort study that should be interpreted with much caution. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) possible selection bias since the patients were not recruited randomly or in a consecutive manner; 3) absence of power analysis; 4) no inclusion or exclusion criteria; 5) did not examine the effect of potential confounding factors on outcomes; and 6) small sample size. A strength was that response was defined.	3
Windebank,K., et al: Post cardiac transplantation lymphoproliferative disorder presenting as t(8;14) Burkitt leukaemia/lymphoma treated with low intensity chemotherapy and rituximab. Pediatric Blood and Cancer Sep 2009; Vol 53, Issue 3; pp. 392-396.		3
Meerbach,A., et al: Monitoring of Epstein-Barr virus load after hematopoietic stem cell transplantation for early intervention in post-transplant lymphoproliferative disease. Journal of Medical Virology Mar 2008; Vol 80, Issue 3; pp. 441-454.		3
LeVasseur,R., et al: Lymphocyte subsets may discern treatment effects in children and young adults with post-transplant lymphoproliferative disorder. Pediatric Transplantation Oct 2003; Vol 7, Issue 5; pp. 370-375.		3

Ocheni,S., et al: EBV reactivation and post transplant lymphoproliferative disorders following allogeneic SCT. Bone Marrow Transplantation 2008; Vol 42, Issue 3; pp. 181-186.		3
Ranganathan,S., et al: Hodgkin-like posttransplant lymphoproliferative disorder in children: Does it differ from posttransplant Hodgkin lymphoma?. Pediatric and Developmental Pathology 2004; Vol 7, Issue 4; pp. 348-360.		3
Orjuela,M., et al: A pilot study of chemoimmunotherapy (cyclophosphamide, prednisone, and rituximab) in patients with post-transplant lymphoproliferative disorder following solid organ transplantation. Clinical Cancer Research Oct 01, 2003; Vol 9, Issue 10 II; pp. 3945s-3952s.		1
Taj,M.M., et al: Long-term outcome for immune suppression and immune related lymphoproliferative disorder: prospective data from the United Kingdom Children's Leukaemia and Cancer Group registry 1994-2004. Leukemia & Lymphoma Dec 13, 2011; Vol E Pub, p. E Pub.		2
Worth,A., et al: Pre-emptive rituximab based on viraemia and T cell reconstitution: A highly effective strategy for the prevention of Epstein-Barr virus-associated lymphoproliferative disease following stem cell transplantation. British Journal of Haematology Nov 2011; Vol 155, Issue 3; pp. 377-385.		1

Jagadeesh,D., et al: Post Transplant Lymphoproliferative Disorders: Risk, Classification, and Therapeutic Recommendations. Curr Treat Options Oncol Jan 13, 2012; Vol E Pub, p. E Pub.		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)

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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	Gerald J. Robbins, 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	---	---		B
Edward P. Balaban, DO	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	Certainly appears effective in an otherwise essentially poorly treated complication with few treatment alternatives and a high mortality	N/A
James E. Liebmann, MD	Effective	Class I - Recommended	While it would be ideal to have the results of COG ANHL 0221, the experience published to date shows that Rituximab is effective in this disorder. Additionally, Rituximab can reduce or even eliminate the need for chemotherapy treatment of post-transplant LPD.	N/A

Gerald J. Robbins, MD	Effective	Class IIa - Recommended, In Most Cases	Strength of evidence is limited by small studies with open label design, etc, but this is a rare disorder and true blinded randomized would be unethical and take an unacceptably long time to complete. Consensus appears to be in favor of inserting this into algorithm of treatment.	N/A
Keith A. Thompson, MD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	None	N/A
John M. Valgus, PharmD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	Although data is retrospective, existing evidence all suggests efficacy and safety on this patient population.	N/A