TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Rituximab

INDICATION: Thrombotic thrombocytopenic purpura, in combination with plasma exchange

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: **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)]

TRUVEN HEALTH ANALYTICS

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Froissart A, Buffet M, Veyradier A, et al. Efficacy and safety of first-line rituximab in severe, acquired thrombotic thrombocytopenic purpura with a suboptimal response to plasma exchange. Experience of the French Thrombotic Microangiopathies Reference Center. Crit Care Med 2012;40(1):104-111.	Study methodology comments: This was a prospective observational study using historical controls. There was a low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcomes. Data for historical controls was gathered from medical records.	S
Scully M, McDonald V, Cavenagh J, et al. A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. Blood 2011;118(7):1746-1753.	Study methodology comments: This was a prospective observational study using historical controls. There was a low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcomes. Data for historical controls was gathered from medical records.	S
Westwood,J.-P., Webster,H., Mcguckin,S., et al: Rituximab for thrombotic thrombocytopenic purpura: Benefit of early administration during acute episodes and use of prophylaxis to prevent relapse. Journal of Thrombosis and Haemostasis 2013; Vol 11, Issue 3; pp. 481-490		2
Provan,D., Butler,T., Evangelista,M.L., et al: Activity and safety profile of low-dose rituximab for the treatment of autoimmune cytopenias in adults. Haematologica Dec 2007; Vol 92, Issue 12; pp. 1695-1698		3

Fakhouri,F., Vernant,J.P., Veyradier,A., et al: Efficiency of curative and prophylactic treatment with rituximab in ADAMTS13-deficient thrombotic thrombocytopenic purpura: a study of 11 cases. Blood Sep 15, 2005; Vol 106, Issue 6; pp. 1932-1937		3
Scully,M., Cavenagh,J.D., Hunt,B., et al: A phase II study to assess the safety, efficacy and tolerability of rituximab (mabthera) in combination with plasma exchange in patients with acute thrombotic thrombocytopenic purpura (TTP). Blood Nov 19, 2010; Vol 116, Issue 21		3
Jatinder,G., Lima,J.L.O., Adamski,J., et al: Rituximab does not prevent relapse in patients with thrombotic thrombocytopenic purpura. Blood Nov 16, 2012; Vol 120, Issue 21. Date of Publication; p. 1		3
Cataland,S.R.: 3 Rs: Rituximab, remission, relapse. Blood Aug 18, 2011; Vol 118, Issue 7; pp. 1711-1712		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	James E. Liebmann, MD	None
Stacy LaClaire, PharmD	None	Jeffrey A. Bubis, DO	Other payments: Dendreon
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

James E. Liebmann, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	Treatment of TTP is unsatisfying for a variety of reasons. The diagnosis of the disease is difficult, and the two studies submitted for review used somewhat different criteria for inclusion. Note that both studies tried to include only acquired, autoimmune TTP so use of rituximab based on these studies should be limited to that specific group of patients with microangiopathic hemolytic anemia. Current standard treatment utilizes plasmapheresis/exchange and it is sensible to add in a new agent to that standard, particularly in patients who have a suboptimal response to plasmapheresis.The benefits of rituximab in these studies were modest, though side effects were also minimal. There probably are some patients with TTP who benefit from rituximab. At present, however, it is not possible to identify those who will do better with rituximab as opposed to standard treatment alone.	N/A
Jeffrey A. Bubis, DO	Ineffective	Class III - Not Recommended	Overall outcomes were unchanged by the drug, which added expense and potential toxicities.	N/A
Gerald J. Robbins, MD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	This is a rare illness with devastating prognosis. Typical phase 3 studies would be difficult and inappropriate. Would certainly rate a “evidence favoring efficacy” and “recommended in most cases” status based upon current studies and if patient has early refractory disease.	N/A

Keith A. Thompson, MD	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	TTP is such a difficult disease to treat, even modest improvement may be a reason to consider rituximab.	N/A
John M. Valgus, PharmD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	Although these trials are by no means robust, they do demonstrate positive clinical outcomes with the addition of rituximab in this setting.	N/A