TRUVEN HEALTH ANALYTICS
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COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 4/19/2018

PACKET: 1667

DRUG: Ruxolitinib Phosphate

USE: Graft versus host disease following allogeneic stem cell transplantation, steroid-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: C, L, 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
Zeiser,R., et al: Ruxolitinib in corticosteroid-refractory graft-versus-host disease after allogeneic stem cell transplantation: A multicenter survey. Leukemia Oct 01, 2015; Vol 29, Issue 10; pp. 2062-2068.	Comments: This was an international cohort study that included 19 sites. This cohort was selected by including all patients that were reported to receive ruxolitinib for aGVHD or cGVHD by the different stem cell transplant centers and no reported patient was excluded. Data was gathered prospectively for research purposes. Histological GVHD grading was performed on the basis of a published staging system and clinical grading was according to criteria for aGVHD or cGVHD. The median follow-up time was 26.5 (3–106) weeks for SR-aGVHD patients. The median follow-up was 22.4 (3–135) weeks for cGVHD patients. A major caveat of the study was the absence of a control group or active comparator. There was low risk of bias associated with selection of cohorts and assessment of outcomes. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	S
Zeiser R, et al. Long-term follow-up of patients with corticosteroid-refractory graft-versus-host disease treated with ruxolitinib. Blood. 2016;128:4561.		S
Ferreira,A.M., et al: Ruxolitinib in steroid-refractory chronic graft-versus-host disease: experience of a single center. Bone Marrow Transplant. Jan 12, 2018;	Comments: This was an retrospective cohort study that included 20 patients with steroid-refractory cGVHD who received RUX therapy. A major caveat of the study was the absence of a control group or active comparator. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Treatment responses were evaluated at 1, 3, and 6 months after starting ruxolitinib and were categorized according to the NIH 2014 criteria. The median follow-up time was 12 (range, 4–19) months. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	3

Khoury,H.J., et al: Ruxolitinib: a steroid sparing agent in chronic graft-versus-host disease. Bone Marrow Transplantation Jan 24, 2018	Comments: This was a retrospective cohort study that prospectively collected data on 19 patients with cGVHD who received salvage RUX therapy. A major caveat of the study was the absence of a control group or active comparator. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Grading of cGVHD and response (complete (CR) and partial (PR) organ based on clinician assessments) was performed by clinicians with extensive transplant experience, and according to the 2014 NIH Consensus Conference Criteria for cGVHD. There was a median follow-up of 17 months (range, 3–25) from prednisone discontinuation/reduction to physiologic doses. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	S
Khandelwal,P., et al: Ruxolitinib as salvage therapy in steroid-refractory acute graft-versus-host sisease in pediatric hematopoietic stem cell transplant patients. Biology of Blood and Marrow Transplantation 2017; Vol 23, Issue 7; pp. 1122-1127.		1
Hurabielle,C., et al: Efficacy and tolerance of ruxolitinib in refractory sclerodermatous chronic graft-versus-host disease. British Journal of Dermatology 2017; Vol 177, Issue 5; pp. e206-e208.	Comments: This was a retrospective cohort study that included twelve patients with severe sclerodermatous cGVHD and were refractory to corticosteroids and at least one other immunosuppressive drug. A major caveat of the study was the absence of a control group or active comparator. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. They used the Rodnan skin score (mRSS) to classify patients and assess response. The following clinical and biological features were assessed at diagnosis and every 3 months: mRSS, photographic range of motion (P-ROM),5 tolerance of the treatment, and T- and B-lymphocyte subpopulations. Patients were followed for up to six months. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	3

Assouan,D., et al: Ruxolitinib as a promising treatment for corticosteroid-refractory graft-versus-host disease. British Journal of Haematology 2017; Vol Epub, p. Epub. Pubmed ID: 28444730	Comments: This was an retrospective cohort study that included ten patients with steroid-refractory GVHD who received RUX therapy. A major caveat of the study was the absence of a control group or active comparator. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. Acute GVHD was staged according to the Glucksberg system (Rowlings et al, 1997). Overlap syndrome was defined as the concomitant occurrence of features of chronic GVHD and acute GVHD, according to the National Institutes of Health consensus criteria. With a median follow-up of 134 days, median survival of the cohort study was not reached. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	3
Maldonado,M.S., et al: Compassionate use of ruxolitinib in acute and chronic graft versus host disease refractory both to corticosteroids and extracorporeal photopheresis. Experimental Hematology and Oncology 2017; Vol 6, Issue 1; p. 32.		3
Barabanshikova,M.V., et al: Posttransplant ruxolitinib combined with cyclophosphamide for graft versus host disease prophylaxis and relapse prevention in patients with myelofibrosis. Cellular Therapy and Transplantation 2016; Vol 5, Issue 3; pp. 15-17.		3
Mori,Y., et al: Ruxolitinib treatment for GvHD in patients with myelofibrosis. Bone Marrow Transplantation 2016; Vol 51, Issue 12; pp. 1584-1587		3

Maffini,E., et al: Ruxolitinib in steroid refractory graft-vs.-host disease: A case report. Journal of Hematology and Oncology Aug 08, 2016; Vol 9, Issue 1; p. 67.		3
Poyatos-Ruiz,L.L., et al: Off-label use of ruxolitinib in refractory graft-versus-host disease after allogenic stem cell transplantation. Value in Health Nov 01, 2016; Vol 19, Issue 7; p. A576.		4
Jagasia,M., et al: Ruxolitinib for the treatment of patients with steroid-refractory GVHD: an introduction to the REACH trials. Immunotherapy. Jan 10, 2018		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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases		B
John D Roberts	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	One prospective and several retrospective series show improvements in steroid-refractory acute and chronic graft versus host disease with acceptable side effects following initiation of ruxolitinib. Although evidence from randomized controlled trials would be preferred, on the basis of these reports ruxolitinib is a reasonable treatment option.	N/A

Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	The use of Ruxolitinib to prevent graft versus host disease in patients who have received stem cell transplant appears to be effective with a positive overall response rate. A less of a dependence on steriods was also demonstrated. There was a higher incidence of adverse reactions that the authors of the studies downplayed. The studies were quite small as well.	N/A
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	Observational studies have identified Ruxolitinib to have clinical activity in steroid-refractory graft-versus-host disease with acceptable toxicity. In a retrospective survey of 95 patients among 19 transplant centers, an overall response rate of 81% was observed.	N/A