TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 6/5/2018

PACKET: 1669

DRUG: Pegaspargase

USE: Extranodal NK/T-cell lymphoma, nasal type

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, E, 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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Li,X., et al: DDGP versus SMILE in newly diagnosed advanced natural killer/T-cell lymphoma: a randomized controlled, multicenter, open-label study in China. Clin Cancer Res Nov 01, 2016; Vol 22, Issue 21; pp. 5223-5228.	Comments: This was a randomized, open-label, multicenter study that compared the efficacy and safety of DDGP regimen with SMILE in patients with newly diagnosed ENKL in III–IV stages. At enrollment, all biopsies were independently reviewed and confirmed by more than two pathologists in accordance withWHO2008 morphologic, immunophenotypic, and genetic criteria. Researchers used standardized scales to measure outcomes and assessed the effect of potential confounders. Overall, this study was at low risk of biases associated with poor random sequence generation, lack of blinding (for objective outcomes only), incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor allocation concealment was unclear and not discussed in the paper. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	S
Wang,J.H., et al: Analysis of the efficacy and safety of a combined gemcitabine, oxaliplatin and pegaspargase regimen for NK/T-cell lymphoma. Oncotarget. Jun 07, 2016; Vol 7, Issue 23; pp. 35412-35422.	Comments: This was a retrospective analysis. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The median follow-up time was 17 months, with a range of 1 month to 51 months. All subjects were included in the analyses. Statistical analyses were performed to assess the effect of potential confounding factors on outcomes. The results should be interpreted with caution since the study lacked a control group.	S
Xu,P.-P., et al: A phase II study of methotrexate, etoposide, dexamethasone and pegaspargase sandwiched with radiotherapy in the treatment of newly diagnosed, stage IE to IIE extranodal natural-killer/T-cell lymphoma, nasal-type. EBioMedicine Nov 01, 2017; Vol 25, pp. 41-49.	Comments: This was a phase 2, open-label, prospective study that included 40 newly diagnosed ENKTL patients who received MESA chemotherapy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Two patients withdrew from the study early but achieved CR after treatment without disease progression or death. They were not included in the analyses. The median follow-up of early and advanced-stage patients was 26.5 and 11.7 months, respectively. Statistical analyses were performed to assess the effect of potential confounding factors on outcomes. The results should be interpreted with caution since the study lacked a control group.	S

Yang,L., et al: Retrospective study of modified SMILE chemotherapy for advanced-stage, relapsed, or refractory extranodal natural killer (NK)/T cell lymphoma, nasal type. Med Oncol Dec 2013; Vol 30, Issue 4; p. 720.	Comments: This was a retrospective study that assessed the impact of two treatment regimens on clinical response and survival among 42 ENKL patients. All diagnoses were confirmed by at least two experienced pathologists.There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. Patients were followed for up to 25 months. All subjects were included in the analyses.	S
Zhang,L., et al: The DDGP (cisplatin, dexamethasone, gemcitabine, and pegaspargase) regimen for treatment of extranodal natural killer (NK)/T-cell lymphoma, nasal type. Oncotarget. Sep 06, 2016; Vol 7, Issue 36; pp. 58396-58404.		3
Zhang,L., et al: Efficacy and safety of cisplatin, dexamethasone, gemcitabine and pegaspargase (DDGP) regimen in newly diagnosed, advanced-stage extranodal natural killer/T-cell lymphoma: interim analysis of a phase 4 study NCT01501149. Oncotarget. Aug 23, 2016; Vol 7, Issue 34; pp. 55721-55731.	Comments: This was a retrospective analysis on 80 patients who received DDGP chemotherapy. Before treatment, hematoxylin-eosin (HE)-stained sections from all patients were histologically reviewed and confirmed by hematopathologists from our institution based on the WHO classification. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The median follow-up time was 20 months. All subjects were included in the analyses. The results should be interpreted with caution since the study lacked a control group.	3
Li,J.-W., et al: Efficacy and tolerance of GELOXD/P-GEMOXD in newly diagnosed nasal-type extranodal NK/T-cell lymphoma: A multicenter retrospective study. Eur J Haematol Mar 01, 2018; Vol 100, Issue 3; pp. 247-256.	Comments: This was a multicenter retrospective study that included two treatment arms, P-GEMOXD and GELOXD. There was low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcome. Data was gathered from medical records. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. All subjects were included in the analyses.	3

Jing,X.M., et al: Efficacy and tolerance of pegaspargase, gemcitabine and oxaliplatin with sandwiched radiotherapy in the treatment of newly-diagnosed extranodal nature killer (NK)/T cell lymphoma. Leuk Res. Aug 2016; Vol 47, pp. 26-31	Comments: This was a retrospective analysis on 38 patients with newly diagnosed ENKTL who received P-Gemox chemotherapy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The median follow-up time was 15.5 months(range, 2–42 months). All subjects were included in the analyses. Statistical analyses were performed to assess the effect of potential confounding factors on outcomes. The results should be interpreted with caution since the study lacked a control group.	2
Wang,J.H., et al: Efficacy of combined gemcitabine, oxaliplatin and pegaspargase (P-gemox regimen) in patients with newly diagnosed advanced-stage or relapsed/refractory extranodal NK/T-cell lymphoma. Oncotarget. May 17, 2016; Vol 7, Issue 20; pp. 29092-29101.	Comments: This was a retrospective analysis on 35 patients with newly diagnosed advanced stage or relapsed/refractory ENKTLL who received P-Gemox chemotherapy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The median follow-up time was 28 months (range, 9–50 months). All subjects were included in the analyses. Statistical analyses were performed to assess the effect of potential confounding factors on outcomes. The results should be interpreted with caution since the study lacked a control group.	2
Wei,W., et al: Effectiveness of pegaspargase, gemcitabine, and oxaliplatin (P-GEMOX) chemotherapy combined with radiotherapy in newly diagnosed, stage IE to IIE, nasal-type, extranodal natural killer/T-cell lymphoma. Hematology Jul 2017; Vol 22, Issue 6; pp. 320-329.	Comments: This was a retrospective analysis on 35 patients with newly diagnosed ENKTL who received P-Gemox chemotherapy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The median follow-up time for the 35 patients was 36 months (range, 5–59 months). All subjects were included in the analyses. Statistical analyses were performed to assess the effect of potential confounding factors on outcomes. The results should be interpreted with caution since the study lacked a control group.	2
Bi,X.W., et al: Radiotherapy and PGEMOX/GELOX regimen improved prognosis in elderly patients with early-stage extranodal NK/T-cell lymphoma. Ann.Hematol. Sep 2015; Vol 94, Issue 9; pp. 1525-1533.		3

Liang,R., et al: A phase 2 study of methotrexate, etoposide, dexamethasone, and pegaspargase chemotherapy for newly diagnosed, relapsed, or refractory extranodal natural killer/T-cell lymphoma, nasal type: a multicenter trial in Northwest China. Hematol.Oncol. Dec 2017; Vol 35, Issue 4; pp. 619-629.	Comments: This was a multicenter retrospective analysis on 46 consecutive patients with histologically confirmed NKTCL who received MESA chemotherapy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered from medical records. The mean duration of follow-up was 12.3 ± 7.5 months (range: 2-24 months) for OS and 10.7 ± 7.2 months (range: 0-24 months) for PFS. All subjects were included in the analyses. cThe results should be interpreted with caution since the study lacked a control group.	2
Yao,Y.-Y., et al: Retrospective Study of Pegaspargase, Gemicitabine, Oxaliplatin and Dexamethasone (Peg-GemOD) as a First-Line Therapy for Advanced-Stage Extranodal NK/T Cell Lymphoma. Indian J Hematol Blood Transfus 2017; Vol 33, Issue 1; pp. 74-81		3
Ding,H., et al: High-dose methotrexate, etoposide, dexamethasone and pegaspargase (MEDA) combination chemotherapy is effective for advanced and relapsed/refractory extranodal natural killer/T cell lymphoma: a retrospective study. Int J Hematol. Aug 2015; Vol 102, Issue 2; pp. 181-187.		3
Li,L., et al: Efficacy of a pegaspargase-based regimen in the treatment of newly-diagnosed extranodal natural killer/T-cell lymphoma. Neoplasma. 2014; Vol 61, Issue 2; pp. 225-232.		3

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	Effective	Class I: Recommended		B
John D Roberts	Effective	Class I: Recommended	In several trials involving both chemotherapy alone for advanced disease and combined chemoradiotherapy for localized disease, combination chemotherapy regimens incorporating pegaspargase yield high response and overall survival rates in extranodal NK/T-cell lymphoma, nasal type. Results were superior to an L-asparaginase containing regimen in one small prospective, randomized study.	N/A

Jeffrey Klein	Evidence Favors Efficacy	Class I: Recommended	The use of Pegaspargase in combination with various other chemotheraputic agents to treat extranodal NK/T-cell lymphoma has been demonstrated to have a good progression free survival in these patients. All of the studies were small. There was a considerable degree of toxicity documented that the authors of all the studies downplay	N/A
Richard LoCicero	Effective	Class I: Recommended	Multiple clinical trials have established the efficacy of pegaspargase-containing chemotherapy regimens for the treatment of Extranodal NK/T-cell lymphoma, nasal type. Treatment was more effective than comparator regimens with less toxicity.	N/A