TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Gemcitabine hydrochloride

INDICATION: Mantle cell lymphoma, relapsed or refractory, as combination therapy

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**
*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
Morschhauser,F., et al: Phase II study of gemcitabinedexamethasone with or without cisplatin in relapsed or refractory mantle cell lymphoma. Annals of Oncology Feb 2007; Vol 18, Issue 2; pp. 370-375.	Study methodology comments: This was an un-randomized, open-label, time-series trial that included two regimens based on age. This was not designed to be a comparative trial. A major weakness of the study was the absence of a control group which would have controlled for confounds. Additional weaknesses included 1) open-label study without the use of independent reviewers; 2) possible selection bias since recruitment was not done randomly or consecutively; 3) absence of a power analysis; 4) did not examine the effect of potential confounding factors on outcomes; and 5) small sample size. Strengths included: 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary outcomes and clinical response; 3) had both inclusion and exclusion criteria; 4) presented 95% confidence intervals; and 5) confirmed diagnosis.	S
Hitz,F., et al: A multicentre phase II trial of gemcitabine for the treatment of patients with newly diagnosed, relapsed or chemotherapy resistant mantle cell lymphoma: SAKK 36/03. Hematological Oncology Sep 2009; Vol 27, Issue 3; pp. 154-159.	Study methodology comments: This was an open-label time-series trial that was conducted in a two-stage design. Due to a low response rate during the first stage, the trial was discontinued. However, eight more subjects were enrolled. A major weakness of the study was the absence of a control group which would have controlled for confounds. Additional weaknesses included 1) open-label study without the use of independent reviewers; 2) possible selection bias since recruitment was not done randomly or consecutively; 3) did not examine the effect of potential confounding factors on outcomes; and 4) small sample size. Strengths included: 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) had both inclusion and exclusion criteria; 3) defined response; 4) presented 95% confidence intervals; and 5) confirmed diagnosis.	1
Garbo,LE., et al: Results of a Phase II trial of gemcitabine, mitoxantrone, and rituximab in relapsed or refractory mantle cell lymphoma. Investigational New Drugs Oct 2009; Vol 27, Issue 5; pp. 476-481.	Study methodology comments: This was an open-label time-series trial that should be interpreted with caution. A major weakness of the study was the absence of a control group which would have controlled for confounds. Additional weaknesses included 1) open-label study without the use of independent reviewers; 2) possible selection bias since recruitment was not done randomly or consecutively; 3) did not examine the effect of potential confounding factors on outcomes; and 4) small sample size. Strengths included: 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) had both inclusion and exclusion criteria; 3) defined response; 4) presented 95% confidence intervals; 5) confirmed diagnosis; 6) defined primary and secondary outcomes; 7) power analysis; and 8) confirmed response at 4 weeks.	S

Rodriguez,J., et al: Rituximab, gemcitabine and oxaliplatin: an effective regimen in patients with refractory and relapsing mantle cell lymphoma. Leukemia & Lymphoma Nov 2007; Vol 48, Issue 11; pp. 2172-2178.	Study methodology comments: This was an open-label time-series trial that should be interpreted with caution. A major weakness of the study was the absence of a control group which would have controlled for confounds. Additional weaknesses included 1) open-label study without the use of independent reviewers; 2) possible selection bias since recruitment was not done randomly or consecutively; 3) absence of power analysis; 4) did not present 95% confidence intervals; and 5) small sample size. Strengths included: 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) had both inclusion and exclusion criteria; 3) defined response; 4) assessed the effect of potential confounding factors on outcomes; 5) confirmed diagnosis; and 6) confirmed response at 4 weeks.	S
Dumontet,C., et al: Gemcitabine as a single agent in the treatment of relapsed or refractory low-grade non- Hodgkin's lymphoma. British Journal of Haematology Jun 2001; Vol 113, Issue 3; pp. 772-778.	Study methodology comments: This was an open-label time-series trial 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 confounds. Additional weaknesses included 1) open-label study without the use of independent reviewers; 2) possible selection bias since recruitment was not done randomly or consecutively; 3) absence of power analysis; 4) did not assess the effect of potential confounding factors on outcomes; and 5) small sample size. Strengths included: 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) had both inclusion and exclusion criteria; 3) defined response; 4) presented 95% confidence intervals; and 5) confirmed diagnosis.	3
Corazzelli,G.: Gemcitabine, ifosfamide, oxaliplatin and rituximab (R-GIFOX), a new effective cytoreductive/mobilizing salvage regimen for relapsed and refractory aggressive non-Hodgkin's lymphoma: Results of a pilot study. Annals of Oncology May 01, 2006; Vol 17, Issue SUPPL. 4; pp. iv18-iv24.		3
Savage,D.G., et al: Gemcitabine for relapsed or resistant lymphoma. Annals of Oncology May 2000; Vol 11, Issue 5; pp. 595-597.		3
Park,B.B., et al: Salvage therapy with gemcitabine, ifosfamide, dexamethasone, and oxaliplatin (GIDOX) for B-cell non-Hodgkin's lymphoma: a consortium for improving survival of lymphoma (CISL) trial. Invest New Drugs Sep 16, 2009; Vol E Pub, p. 1.		3
Perrotti,A.P.: Vinorelbine and gemcitabine as salvage treatment in advanced and very poor prognosis non- Hodgkin's lymphoma patients. Annals of Hematology Jun 01, 2008; Vol 87, Issue 6; pp. 493-494.		3

Ng,M.: Gemcitabine, cisplatin and methylprednisolone (GEM-P) is an effective salvage regimen in patients with relapsed and refractory lymphoma. Br J Cancer Apr 25, 2005; Vol 92, Issue 8; pp. 1352-1357.		3
Chau,I., et al: Gemcitabine, cisplatin and methylprednisolone chemotherapy (GEM-P) is an effective regimen in patients with poor prognostic primary progressive or multiply relapsed Hodgkin's and non-Hodgkin's lymphoma. British Journal of Haematology Mar 2003; Vol 120, Issue 6; pp. 970-977.		3
Sampol,A., et al: Gemcitabine and oxaliplatinum: an effective regimen in a patient with progressive refractory mantle cell lymphoma. Leukemia & Lymphoma Jun 2004; Vol 45, Issue 6; pp. 1289-1291.		3
Morschhauser,F., et al: Gemcitabine with Dexamethasone+/-Cisplatin in Patients with Relapsing/Refractory Mantle Cell Lymphoma. Blood Nov 16, 2002; Vol 100, Issue 11.		3
Gopal,AK., et al: A Prospective Multicenter Phase II Study by the Puget Sound Oncology Consortium (PSOC) of Gemcitabine (G), Carboplatin (C), Dexamethasone (D), and Rituximab (R) in Patients with Relapsed/Refractory Lymphoma. Blood Nov 16, 2008; Vol 112, Issue 11; p. 896.		3
Verhoef,E.G., et al: Phase 3 Study of Patients with Relapsed, Refractory Mantle Cell Lymphoma: Comparison of Treatment with Temsirolimus Vs Investigator'S Choice Therapy. Haematologica-the Hematology Journal Jun 2008; Vol 93, Issue 1; pp. 174-174.		3
El Gnaoui, T., et al: Rituximab, gemcitabine and oxaliplatin (R-GEMOX): A promising regimen for refractory/relapsed B-cell lymphoma. Blood Nov 16, 2004; Vol 104, Issue 11, Part 1; p. 681A.		3

El Gnaoui, T., et al: Rituximab, gemcitabine and oxaliplatin (R-GEMOX): A promising salvage regimen for refractory/relapsed B-cell lymphoma. A pilot Study. Blood Nov 16, 2003; Vol 102, Issue 11; p. 299b		3
Garbo,L.E., et al: Results of a nonrandomized, openlabel, phase II study of combined gemcitabine, mitoxantrone, and rituximab in relapsed or refractory mantle cell lymphoma. Blood Nov 16, 2007; Vol 110, Issue N11,2; pp. 183B-183B.		3
Hitz,F., et al: A multicentre phase II trial testing gemcitabine in the treatment of patients with newly diagnosed, relapsed or chemotherapy resistant mantle cell lymphoma: SAKK 36/03. Blood Nov 16, 2007; Vol 110, Issue N11,2; pp. 183B-183B.		3
Romaguera,J.E., et al: High (95%) response rates in relapsed/refractory mantle cell lymphoma after RHCVAD alternating with R-methotrexate/cytarabine (RM- A). Blood Nov 16, 2005; Vol 106, Issue 11, Part 1; p. 688A.		3
Hoffmann,M., et al. Phase I/II Study for the Effectivity of Rituximab, Gemcitabin and Oxaliplatin in Relapsed Indolent Lymphoma – An Interim Report. Blood (ASH Annual Meeting Abstracts), Nov 2009; 114: 3700.		3
Gopal, A. K., et al. A Prospective Multicenter Phase II Study by the Puget Sound Oncology Consortium (PSOC) of Gemcitabine (G), Carboplatin (C), Dexamethasone (D), and Rituximab (R) in Patients with Relapsed/Refractory Lymphoma Blood (ASH Annual Meeting Abstracts), Nov 2008; 112: 2		3
El Gnaou,T., et al. Rituximab, Gemcitabine and Oxaliplatin (R-GEMOX): A Promising Regimen for Refractory/Relapsed B-Cell Lymphoma. Blood (ASH Annual Meeting Abstracts), Nov 2004; 104: 2483.		3

Kirschbaum, M., et al. Phase I Study of Bortezomib in Combination with Gemcitabine in Relapsed/Refractory Intermediate Grade B-Cell and Mantle Cell Non-Hodgkin's Lymphoma. Blood (ASH Annual Meeting Abstracts), Nov 2009; 114: 1682		3
Morschhauser, F., et al. Gemcitabine with dexamethasone +/- cisplatin in patients with previously treated CLL and mantle cell lymphoma. 2002 ASCO abstract.		3
Romaguera,J.E.: Mantle cell lymphoma: Frontline and salvage therapy. Current Hematologic Malignancy Reports Dec 01, 2008; Vol 3, Issue 4; pp. 204-209.		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)

TRUVEN HEALTH ANALYTICS

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Amy Hemstreet, PharmD	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	John M. Valgus, PharmD	None
		Gerald J. Robbins, MD	None
		Keith A. Thompson, 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 the data leans toward Gemcitabine having an efficacious role - studies and evidence remains small and difficult to comment on any further.	N/A
James E. Liebmann, MD	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	The activities of the various regimens presented in these studies are believable and consistent. However, only a total of 60 patients are represented by these trials, raising the question of how broadly applicable the studies are to a general population of patients with recurrent MCL.	N/A
John M. Valgus, PharmD	Evidence Favors Efficacy	Class IIa Recommended, In Most Cases	Has shown both single agent + combination activity. May be used for refractory pts w/ Mantle Cell	N/A
Gerald J. Robbins, MD	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	Response rates are reasonable given significant hematologic toxicity and duration of responses were short. Needs further study.	N/A

Keith A. Thompson, MD	Evidence Favors Efficacy	Class IIb Recommended, In Some Cases	None	N/A