TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Cisplatin

INDICATION: Pancreatic cancer, locally advanced or metastatic, first-line therapy in combination with gemcitabine

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, 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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TRUVEN HEALTH ANALYTICS

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Colucci,G., et al: Randomized phase III trial of gemcitabine plus cisplatin compared with single-agent gemcitabine as first-line treatment of patients with advanced pancreatic cancer: the GIP-1 study. J Clin Oncol Apr 01, 2010; Vol 28, Issue 10; pp. 1645-1651	Study methodology comments: This was a randomized, open-label, phase III trial. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included: 1) had both inclusion and exclusion criteria; 2) defined clinical benefit and tumor response; 3) explained method of randomization; 4) compared baseline characteristics of groups; 5) analyzed the intent-to-treat population; 6) defined primary and secondary outcomes; 7) conducted power analysis; and 8) presented 95% confidence intervals. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; and 2) open-label design without the use of independent reviewers.	S
Heinemann,V., et al: Randomized phase III trial of gemcitabine plus cisplatin compared with gemcitabine alone in advanced pancreatic cancer. J Clin Oncol Aug 20, 2006; Vol 24, Issue 24; pp. 3946-3952.	Study methodology comments: This was a randomized, open-label, phase III trial. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included: 1) presented eligibility criteria; 2) defined tumor response and outcome measures; 3) compared baseline characteristics of groups; 4) analyzed the intent-to-treat population; 5) defined primary and secondary outcomes; 6) conducted power analysis; and 7) presented 95% confidence intervals. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; 2) open-label design without the use of independent reviewers; and 3) did not discuss method of randomization.	S
Colucci,G., et al: Gemcitabine alone or with cisplatin for the treatment of patients with locally advanced and/or metastatic pancreatic carcinoma: a prospective, randomized phase III study of the Gruppo Oncologia dell'Italia Meridionale. Cancer Feb 15, 2002; Vol 94, Issue 4; pp. 902-910.		3

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Choi,j.H., et al: Gemcitabine versus gemcitabine combined with cisplatin treatment locally advanced or metastatic pancreatic cancer: a retrospective analysis. Cancer Res Treat Mar 2008; Vol 40, Issue 1; pp. 22-26.		3
Bang,S., et al: Phase II study of cisplatin combined with weekly gemcitabine in the treatment of patients with metastatic pancreatic carcinoma. Pancreatology 2006; Vol 6, Issue 6; pp. 635-641.		3
Ko,A.H., et al: Phase II study of fixed dose rate gemcitabine with cisplatin for metastatic adenocarcinoma of the pancreas. J Clin Oncol Jan 20, 2006; Vol 24, Issue 3; pp. 379-385.		3
Cascinu,S., et al: Weekly gemcitabine and cisplatin chemotherapy: a well-tolerated but ineffective chemotherapeutic regimen in advanced pancreatic cancer patients. A report from the Italian Group for the Study of Digestive Tract Cancer (GISCAD). Ann Oncol Feb 2003; Vol 14, Issue 2; pp. 205-208.		3
Philip,P.A., et al: Phase II study of gemcitabine and cisplatin in the treatment of patients with advanced pancreatic carcinoma. Cancer Aug 01, 2001; Vol 92, Issue 3; pp. 569-577.		3
Heinemann,V., et al: Gemcitabine and cisplatin in the treatment of advanced or metastatic pancreatic cancer. Ann Oncol Nov 2000; Vol 11, Issue 11; pp. 1399-1403.		3

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Ueno,H., et al: Phase II study of combination chemotherapy with gemcitabine and cisplatin for patients with metastatic pancreatic cancer. Jpn J Clin Oncol Jul 2007; Vol 37, Issue 7; pp. 515-520.		3
Clayton,A.J., et al: A phase II study of weekly cisplatin and gemcitabine in patients with advanced pancreatic cancer: is this a strategy still worth pursuing?. Pancreas Jan 2006; Vol 32, Issue 1; pp. 51-57.		3
Ko,A.H., et al: A phase II study of fixed-dose rate gemcitabine plus low-dose cisplatin followed by consolidative chemoradiation for locally advanced pancreatic cancer. Int J Radiat Oncol Biol Phys Jul 01, 2007; Vol 68, Issue 3; pp. 809-816. Pubmed		3
Brodowicz,T., et al: Phase II study of gemcitabine in combination with cisplatin in patients with locally advanced and/or metastatic pancreatic cancer. Anticancer Drugs Sep 2000; Vol 11, Issue 8; pp. 623-628.		3
Chauffert,B., et al: Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000-01 FFCD/SFRO study. Ann Oncol Sep 2008; Vol 19, Issue 9; pp. 1592-1599.		1

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Wilkowski,R., et al: Chemoradiotherapy with concurrent gemcitabine and cisplatin with or without sequential chemotherapy with gemcitabine/cisplatin vs chemoradiotherapy with concurrent 5-fluorouracil in patients with locally advanced pancreatic cancer--a multi-centre randomised phase II study. Br J Cancer Dec 01, 2009; Vol 101, Issue 11; pp. 1853-1859.		1
Varadhachary,G.R., et al: Preoperative gemcitabine and cisplatin followed by gemcitabine-based chemoradiation for resectable adenocarcinoma of the pancreatic head. J Clin Oncol Jul 20, 2008; Vol 26, Issue 21; pp. 3487-3495.		1
Haddock,M.G., et al: Gemcitabine, cisplatin, and radiotherapy for patients with locally advanced pancreatic adenocarcinoma: Results of the North Central Cancer Treatment Group Phase II Study N9942. Journal of Clinical Oncology Jun 20, 2007; Vol 25, Issue 18; pp. 2567-2572.		1
Hong,S.P., et al: Weekly full-dose gemcitabine and single-dose cisplatin with concurrent radiotherapy in patients with locally advanced pancreatic cancer. Br J Cancer Mar 11, 2008; Vol 98, Issue 5; pp. 881-887.		1
Wilkowski,R., et al: Concurrent chemoradiotherapy with gemcitabine and cisplatin after incomplete (R1) resection of locally advanced pancreatic carcinoma. Int J Radiat Oncol Biol Phys Mar 01, 2004; Vol 58, Issue 3; pp. 768-772.		1

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Reni,M., et al: Gemcitabine versus cisplatin, epirubicin, fluorouracil, and gemcitabine in advanced pancreatic cancer: a randomised controlled multicentre phase III trial. Lancet Oncol Jun 2005; Vol 6, Issue 6; pp. 369-376.		1
Reni,M., et al: Final results of a prospective trial of a PEFG (Cisplatin, Epirubicin, 5-Fluorouracil, Gemcitabine) regimen followed by radiotherapy after curative surgery for pancreatic adenocarcinoma. Oncology 2005; Vol 68, Issue 2-3; pp. 239-245.		1
Reni,M., et al: Definitive results of a phase II trial of cisplatin, epirubicin, continuous-infusion fluorouracil, and gemcitabine in stage IV pancreatic adenocarcinoma. J Clin Oncol May 15, 2001; Vol 19, Issue 10; pp. 2679-2686.		1
Reni,M., et al: Dose-intense PEFG (cisplatin, epirubicin, 5-fluorouracil, gemcitabine) in advanced pancreatic adenocarcinoma. Cancer Chemother Pharmacol Feb 2007; Vol 59, Issue 3; pp. 361-367.		1
Reni,M., et al: PEFG (cisplatin, epirubicin, 5-fluorouracil, gemcitabine) regimen as second-line therapy in patients with progressive or recurrent pancreatic cancer after gemcitabine-containing chemotherapy. Am J Clin Oncol Apr 2008; Vol 31, Issue 2; pp. 145-150.		1
El-Rayes,B.F., et al: Phase II study of gemcitabine, cisplatin, and infusional fluorouracil in advanced pancreatic cancer. J Clin Oncol Aug 01, 2003; Vol 21, Issue 15; pp. 2920-2925.		1

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Dahan,L., et al: Combination 5-fluorouracil, folinic acid and cisplatin (LV5FU2-CDDP) followed by gemcitabine or the reverse sequence in metastatic pancreatic cancer: final results of a randomised strategic phase III trial (FFCD 0301). Gut Nov 12010; Vol 59, Issue 11; pp. 527-1534.		1
Landry,J., et al: Randomized phase II study of gemcitabine plus radiotherapy versus gemcitabine, 5-fluorouracil, and cisplatin followed by radiotherapy and 5-fluorouracil for patients with locally advanced, potentially resectable pancreatic adenocarcinoma. J Surg Oncol Jun 01, 2010; Vol 101, Issue 7; pp. 587-592.		1
Lutz,M.P., et al: Docetaxel plus gemcitabine or docetaxel plus cisplatin in advanced pancreatic carcinoma: Randomized phase II study 40984 of the European Organisation for Research and Treatment of Cancer Gastrointestinal Group. Journal of Clinical Oncology 2005; Vol 23, Issue 36; pp. 9250-9256.		1
Araneo,M., et al: Biweekly low-dose sequential gemcitabine, 5-fluorouracil, leucovorin, and cisplatin (GFP): a highly active novel therapy for metastatic adenocarcinoma of the exocrine pancreas. Cancer Invest 2003; Vol 21, Issue 4; pp. 489-496.		1

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Ko,A.H., et al: A phase II study evaluating bevacizumab in combination with fixed-dose rate gemcitabine and low-dose cisplatin for metastatic pancreatic cancer: is an anti-VEGF strategy still applicable?. Invest New Drugs Oct 2008; Vol 26, Issue 5; pp. 463-471.		1
Novarino,A., et al: Phase II study of cisplatin, gemcitabine and 5-fluorouracil in advanced pancreatic cancer. Ann Oncol Mar 2004; Vol 15, Issue 3; pp. 474-477.		1
Heinemann,V., et al: Increased survival using platinum analog combined with gemcitabine as compared to single-agent gemcitabine in advanced pancreatic cancer: pooled analysis of two randomized trials, the GERCOR/GISCAD intergroup study and a German multicenter study. Ann Oncol Oct 2007; Vol 18, Issue 10; pp. 1652-1659.		1
Xie,de R., et al: Meta-analysis of inoperable pancreatic cancer: gemcitabine combined with cisplatin versus gemcitabine alone. Chin J Dig Dis 2006; Vol 7, Issue 1; pp. 49-54.		4
Wang,X., et al: Gemcitabine or gemcitabine plus cisplatin for in 42 patients with locally advanced or metastatic pancreatic cancer. Zhonghua Zhong Liu Za Zhi Jul 2002; Vol 24, Issue 4; pp. 404-407.		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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TRUVEN HEALTH ANALYTICS

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Jeffrey A. Bubis, DO	Other payments: Dendreon
Stacy LaClaire, PharmD	None	Edward P. Balaban, DO	None
Felicia Gelsey, MS	None	James E. Liebmann, 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
Jeffrey A. Bubis, DO	Ineffective	Class III: Not Recommended	Increased toxicity without benefit.	N/A
Edward P. Balaban, DO	Ineffective	Class III: Not Recommended	Little data, but what is available supports it's (Cisplatinum's) ineffectiveness	N/A
James E. Liebmann, MD	Ineffective	Class III: Not Recommended	Despite the optimistic tone of the German group in the 2006 JCO paper, the Italians have a more realistic view of the situation when they conclude "the addition of weekly Cisplatin to Gemcitabine did not produce any benefit compared to single agent Gemcitabine." The 2010 study is completely negative. The smaller 2006 trial also showed no improvement in OS and no difference in RR. A modest improvement in PFS in the Cis-Gem ARM is of questionable clinical significance.	N/A
Keith A. Thompson, MD	Ineffective	Class III: Not Recommended	None	N/A

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John M. Valgus, PharmD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	Conflicting data on benefits of addition of Cisplatin. Weight of evidence suggests no benefit however differences in dose and schedule make comparison of trials difficult. More benefit seen in patients with good PS.	N/A

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