TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: OXALIPLATIN

INDICATION: Advanced or metastatic biliary tract cancer, 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, 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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Sharma,A., et al: Best supportive care compared with chemotherapy for unresectable gall bladder cancer: a randomized controlled study. J Clin Oncol Oct 20, 2010; Vol 28, Issue 30; pp. 4581-4586	Study methodology comments: This was an open-label, randomized controlled trial. A major strength of the study was the inclusion of a control group (patients who received best supportive care only). Additional strengths included 1) confirmed diagnosis; 2) eligibility criteria; 3) defined primary and secondary endpoints; 4) power analysis; 5) defined response; 6) compared baseline characteristics of groups; and 7) presented 95% confidence intervals. Weaknesses were 1) open-label design without the use of independent reviewers; 2) did not discuss the method of randomization; and 3) possible selection bias since the patients were not recruited in a random or consecutive manner.	S
Lee,J., et al: Gemcitabine and oxaliplatin with or without erlotinib in advanced biliary-tract cancer: a multicentre, open-label, randomised, phase 3 study. Lancet Oncol Feb 2012; Vol 13, Issue 2; pp. 181-188.	Study methodology comments: This was an open-label, randomized controlled trial with many strengths. There were two major strengths of the study. First, a control group was included. Second, the effect of many confounding factors were controlled through the study design and analyses. Additional strengths included 1) confirmed diagnosis; 2) eligibility criteria; 3) defined primary and secondary endpoints; 4) power analysis; 5) defined response; 6) responses were confirmed at 4 weeks; 7) allocation concealment; 8) compared baseline characteristics of groups; 9) presented 95% confidence intervals; 10) randomization was done centrally; and 11) analyzed the intent-to-treat population. Weaknesses were 1) open-label design without the use of independent reviewers; and 2) possible selection bias since the patients were not recruited in a random or consecutive manner.	S
Jang,J.S., et al: Gemcitabine and oxaliplatin in patients with unresectable biliary cancer including gall bladder cancer: a Korean Cancer Study Group phase II trial. Cancer Chemother Pharmacol Mar 2010; Vol 65, Issue 4; pp. 641-647.	Study methodology comments: This was an open-label, phase II single-arm trial. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; and 2) possible selection bias since the patients were not recruited in a random or consecutive manner. A major strength of the study was that it controlled for the effect of potential confounding factors on outcomes. Other strengths were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary endpoints; 3) defined response; 4) responses were confirmed at 4 weeks; 5) confirmed diagnosis; 6) had both inclusion and exclusion criteria; 7) included 95% confidence intervals; and 8) conducted power analysis.	S

Andre,T., et al: Gemcitabine and oxaliplatin in advanced biliary tract carcinoma: a phase II study. Br J Cancer Sep 16, 2008; Vol 99, Issue 6; pp. 862-867	Study methodology comments: This was an open-label, phase II single-arm trial. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; and 2) possible selection bias since the patients were not recruited in a random or consecutive manner. Strengths were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary objective and response; 3) confirmed diagnosis; 4) had both inclusion and exclusion criteria; 5) confirmed tumor response at 4 weeks; 6) included 95% confidence intervals; 7) conducted power analysis; 8) identified exploratory analysis; and 9) stratified results by gallbladder carcinoma status.	2
Sharma,A., et al: A phase II study of gemcitabine and oxaliplatin (Oxigem) in unresectable gall bladder cancer. Cancer Chemother Pharmacol Feb 2010; Vol 65, Issue 3; pp. 497-502.	Study methodology comments: This was an open-label, phase II single-arm trial. A major weakness of the study was the absence of a control group which would have controlled for many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) did not examine the effect of potential confounding factors on outcomes; and 3) possible selection bias since the patients were not recruited in a random or consecutive manner. Strengths were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary endpoints; 3) defined response; 4) confirmed diagnosis; 5) had both inclusion and exclusion criteria; 6) included 95% confidence intervals; and 7) conducted power analysis.	2
Androulakis,N., et al: Oxaliplatin as first-line treatment in inoperable biliary tract carcinoma - A multicenter phase II study. Oncology 2006; Vol 70, Issue 4; pp. 280-284.		1
Andre,T., et al: Gemcitabine combined with oxaliplatin (GEMOX) in advanced biliary tract adenocarcinoma: a GERCOR study. Ann Oncol Sep 2004; Vol 15, Issue 9; pp. 1339-1343.		3

Nehls,O., et al: Capecitabine plus oxaliplatin as first-line treatment in patients with advanced biliary system adenocarcinoma: a prospective multicentre phase II trial. Br J Cancer Jan 29, 2008; Vol 98, Issue 2; pp. 309-315.		1
Wagner,A.D., et al: Gemcitabine, oxaliplatin and 5-FU in advanced bile duct and gallbladder carcinoma: two parallel, multicentre phase-II trials. Br J Cancer Dec 01, 2009; Vol 101, Issue 11; pp. 1846-1852.		1
Dwary,A.D., et al: A randomized controlled trial (RCT) comparing best supportive care (BSC), 5-FU plus folinic acid (FUFA) and, gemcitabine plus oxaliplatin (Gem-Ox) in management of unresectable gallbladder cancer (GBC). Journal of Clinical Oncology May 20, 2009; Vol 27, Issue 15; p. 1.		3
Thatikonda,C., Miller,A., and Iyer,R.: Meta Analysis of Oxaliplatin-based Combination Chemotherapy for Advanced Gallbladder and Bile Duct Cancers (AGBC). American Journal of Gastroenterology Oct 2010; Vol 105, pp. S72-S72.		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)

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CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	Keith A. Thompson, MD	None
Felicia Gelsey, MS	None	James E. Liebmann, MD	None
		Jeffrey A. Bubis, DO	Other payments: Dendreon
		John M. Valgus, PharmD	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	Data appears that Oxaliplatin may be efficacious in a longer PFS – however toxicity was considerable!	N/A
Keith A. Thompson, MD	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	None	N/A
James E. Liebmann, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	It is difficult to say that anything we do for these cancers is effective. However, there is a well done randomized trial that showed a modest survival benefit from the addition of Cisplatin to Gemcitabine. The Sharma, et al paper in JCO suggests a benefit from Gemox, at least in gall bladder cancer. The Phase II trials of Gemox at least give consistent results. So, in appropriate patents for whom Cisplatin may be contraindicated (e.g, renal insufficiency) Gemox could be considered.	N/A

Jeffrey A. Bubis, DO	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	This is a reasonable agent in recurrent /refractory disease, but there is superior data for alternatives in the front-line setting.	N/A
John M. Valgus, PharmD	Effective	Class IIa - Recommended, In Most Cases	Multiple clinical trials demonstrating activity in this setting. Comparative data proving benefit vs BSC alone. Studies completed in patients with good performance status.	N/A