TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Carboplatin

INDICATION: Ovarian cancer, early-stage epithelial, adjuvant 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: **A, 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)]

TRUVEN HEALTH ANALYTICS

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Trope,C., et al: Randomized study on adjuvant chemotherapy in stage I high-risk ovarian cancer with evaluation of DNA-ploidy as prognostic instrument. Ann Oncol Mar 2000; Vol 11, Issue 3; pp. 281-288.	Study methodology comments: This was a randomized, open-label, comparative trial. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included 1) had inclusion and exclusion criteria; 2) had a control group; 3) compared baseline characteristics of groups; and 4) presented 95% confidence intervals. Weaknesses included 1) partial explanation of method of randomization; 2) open-label design without the use of independent reviewers; 3) absence of a power analysis; 4) wide confidence intervals; and 5) possible selection bias since subjects were not recruited in a random or consecutive manner.	S
Bell,J., et al: Randomized phase III trial of three versus six cycles of adjuvant carboplatin and paclitaxel in early stage epithelial ovarian carcinoma: a Gynecologic Oncology Group study. Gynecol Oncol Sep 2006; Vol 102, Issue 3; pp. 432-439.	Study methodology comments: This was a randomized, open-label, comparative trial. Additional strengths of the study included 1) had inclusion and exclusion criteria; 2) confirmed diagnosis; 3) defined primary endpoint; 4) defined outcomes; 5) controlled for the effect of potential confounding factors on outcomes; 6) power analysis; 7) compared baseline characteristics of groups; and 8) presented 95% confidence intervals. Weaknesses included 1) did not discuss method of randomization; 2) open-label design without the use of independent reviewers; and 3) possible selection bias since subjects were not recruited in a random or consecutive manner.	S
Young,R.C.: Three cycles versus six cycles of adjuvant paclitaxel (Taxol)/carboplatin in early stage ovarian cancer. Semin Oncol Jun 2000; Vol 27, Issue 3 Suppl 7; pp. 8-10.	Study methodology comments: Same study as Bell et al. 2006.	2

Bamias,A, et al: Four cycles of paclitaxel and carboplatin as adjuvant treatment in early-stage ovarian cancer: a six-year experience of the Hellenic Cooperative Oncology Group. BMC Cancer 2006; Vol 6 p228, p. 22888.	Study methodology comments: This was a retrospective cohort study. 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) absence of a power analysis. Strengths were 1) had inclusion and exclusion criteria; 2) examined the effect of some confounding factors on outcome; 3) presented 95% confidence intervals; and 4) reduced possible selection bias by recruiting consecutively presenting patients.	S
Malmstrom,H., Simonsen,E., and Westberg,R.: A phase II study of intraperitoneal carboplatin as adjuvant treatment in early-stage ovarian cancer patients. Gynecol Oncol Jan 1994; Vol 52, Issue 1; pp. 20-25.	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 many potential confounds. Additional weaknesses included 1) open-label design without the use of independent reviewers; 2) possible selection bias since the patients were not recruited randomly or in a consecutive manner; 3) absence of power analysis; and 4) no exclusion criteria. Strengths were 1) confirmed diagnosis; 2) had inclusion criteria; 3) examined the effect of some confounding factors on outcome; and 4) the use of a within-subject design to control for confounding effects of patient characteristics.	3
Trimbos,J.B., et al: International Collaborative Ovarian Neoplasm trial 1 and Adjuvant ChemoTherapy In Ovarian Neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. J Natl Cancer Inst Jan 15, 2003; Vol 95, Issue 2; pp. 105-112.		S

Trimbos JB, et al. Impact of adjuvant chemotherapy and surgical staging in early-stage ovarian carcinoma: European Organisation for Research and Treatment of Cancer-Adjuvant ChemoTherapy in Ovarian Neoplasm trial. J Natl Cancer Inst. 2003 Jan 15;95(2):113-25.	Study methodology comments: This was a randomized, open-label trial that compared adjuvant chemotherapy with no adjuvant chemotherapy. Due to slow accrual and a noted survival benefit in the no-adjuvant arm, the investigators of ICON1 and ACTION agreed to stop accrual after enrolling 450 patients per trial. The investigators of the two trials agreed to conduct a power analysis for an analysis that pooled the data across the two trials. A combined data analysis required 900 total subjects to provide enough events to yield 90% power to detect an increase in absolute 3-year survival of 6%. Therefore, the individual trials were not powered to detect a treatment benefit with adjuvant chemotherapy. Additional strengths of the study included 1) had inclusion and exclusion criteria; 2) had a control group; 3) compared baseline characteristics of groups; 4) presented 95% confidence intervals; 5) confirmed diagnosis; 6) discussed the method of randomization; 7) defined primary and secondary endpoints; 8) preserved the type I error rate; and 9) controlled for the effect of potential confounding factors on outcomes. Weaknesses included 1) some wide confidence intervals; 2) possible selection bias since patients were not recruited in a random or consecutive manner; 3) open-label design without the use of independent reviewers; and 4) had to terminate accrual prematurely and did not meet power requirements to detect treatment benefit for individual trial.	S

Colombo,N., et al: International Collaborative Ovarian Neoplasm trial 1: a randomized trial of adjuvant chemotherapy in women with early-stage ovarian cancer. J Natl Cancer Inst Jan 15, 2003; Vol 95, Issue 2; pp. 125-132.	Study methodology comments: This was a randomized, open-label trial that compared adjuvant chemotherapy with no adjuvant chemotherapy. Due to slow accrual and a noted survival benefit in the no-adjuvant arm, the investigators of ICON1 and ACTION agreed to stop accrual after enrolling 450 patients per trial. The investigators of the two trials agreed to conduct a power analysis for an analysis that pooled the data across the two trials. A combined data analysis required 900 total subjects to provide enough events to yield 90% power to detect an increase in absolute 3-year survival of 6%. Therefore, the individual trials were not powered to detect a treatment benefit with adjuvant chemotherapy. Additional strengths of the study included 1) had inclusion criteria; 2) had a control group; 3) compared baseline characteristics of groups; 4) presented 95% confidence intervals; 5) confirmed diagnosis; 6) discussed the method of randomization; 7) defined primary and secondary endpoints; 8) reduced selection bias since recruited all presenting patients; 9) preserved the type I error rate; and 10) controlled for the effect of potential confounding factors on outcomes. Weaknesses included 1) open-label design without the use of independent reviewers; and 2) had to terminate accrual prematurely and did not meet power requirements to detect treatment benefit for individual trial.	S
Garcia-Saenz,J.A., et al: Platinum-based adjuvant chemotherapy on moderate- and high-risk stage I and II epithelian ovarian cancer patients. Long-term single institution experience and literature review. Clin Transl Oncol Feb 2011; Vol 13, Issue 2; pp. 121-132.		3
Shimada,M., et al: Outcome of patients with early ovarian cancer undergoing three courses of adjuvant chemotherapy following complete surgical staging. Int J Gynecol Cancer Jul 2005; Vol 15, Issue 4; pp. 601-605.		3

Linasmita,V., et al: Epithelial ovarian cancer treated by platinum or platinum analogue with cyclophosphamide: experience in Ramathibodi Hospital. Journal of the Medical Association of Thailand = Chotmaihet thangphaet Jan 1998; Vol 81, Issue 1; pp. 10-16.		1
Lu,M.J., et al: Intraperitoneal therapy as consolidation for patients with ovarian cancer and negative reassessment after platinum-based chemotherapy. Hematology-Oncology Clinics of North America Aug 2003; Vol 17, Issue N4; pp. 969-		1
Skirnisdottir,I., Lindborg,K., and Sorbe,B.: Adjuvant chemotherapy with carboplatin and taxane compared with single drug carboplatin in early stage epithelial ovarian carcinoma. Oncol Rep Nov 2007; Vol 18, Issue 5; pp. 1249-1256.		1
Adams,G., et al: Platinum-based adjuvant chemotherapy for early-stage epithelial ovarian cancer: single or combination chemotherapy?. BJOG - an International Journal of Obstetrics and Gynaecology Nov 2010; Vol 117, Issue 12; pp. 1459-1467.		1
Balbi,G.C., et al: Paclitaxel and carboplatin as outpatient therapy for stage III and IV epithelial ovarian cancer. Panminerva Medica Dec 2001; Vol 43, Issue 4; pp. 263-265.		1

Brown,J.,V, et al: Three-hour paclitaxel infusion and carboplatin is an effective outpatient treatment for stage III epithelial ovarian cancer. Gynecologic Oncology Feb 1998; Vol 68, Issue 2; pp. 166-168.		1
Dizon,Don S., et al: Two for good measure: six versus eight cycles of carboplatin and paclitaxel as adjuvant treatment for epithelial ovarian cancer. Gynecologic Oncology Feb 2006; Vol 100, Issue 2; pp. 417-421.		1
Chen,H.: Combination of docetaxel-carboplatin for adjuvant chemotherapy of epithelial ovarian, primary peritoneal and fallopian tube cancers: A meta-analysis. Chinese-German Journal of Clinical Oncology Aug 01, 2010; Vol 9, Issue 8; pp. 475-481.		4
Markman,M.: An update on the use of intraperitoneal chemotherapy in the management of ovarian cancer. Cancer Journal Mar 01, 2009; Vol 15, Issue 2; pp. 105-109.		4
Markman,M.: Re: "Randomized phase III trial of three versus six cycles of adjuvant carboplatin and paclitaxel in early stage epithelial ovarian carcinoma: a Gynecologic Oncology Group study". Gynecol Oncol Apr 2007; Vol 105, Issue 1; pp. 279-280.		4
Ozols,R.F.: NICE guidelines for ovarian cancer: recommendations versus standard care. Cancer Invest 2004; Vol 22, Issue 5; pp. 815-817.		4

Poveda,Velasco A.: Treatment guidelines in ovarian cancer. Clinical and Translational Oncology Dec 01, 2007; Vol 9, Issue 5; pp. 308-316.		4
Reed,N.: Non-epithelial ovarian cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology May 01, 2010; Vol 21, Issue SUPPL. 5; pp. v31-v36.		4
Malmstrom,H., Larsson,D., Hogberg,T., et al: Intraperitoneal ip carboplatin as adjuvant therapy in early ovarian cancer phase i. Journal of Cancer Research and Clinical Oncology 1990; Vol 116, Issue SUPPL. PART 1; p. 525.	Study methodology comments: Abstract	3
Shafer,A., et al: Improved survival with consolidation chemotherapy after adjuvant paclitaxel and carboplatin in advanced epithelial ovarian cancer. Gynecologic Oncology Feb 2009; Vol 112, Issue N2,1; pp. S135-S136.	Study methodology comments: Abstract	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
Margi Schiefelbein, PA	None	Jeffrey A. Bubis,DO	None
Stacy LaClaire, PharmD	None	Thomas McNeil Beck, MD	None
Felicia Gelsey, MS	None	Keith A. Thompson, MD	None
		Jeffrey F. Patton, 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	Effective	Class I: Recommended	Clear SOC randomized data supports use. Endorsed by guidelines because of this.	N/A
Thomas McNeil Beck, MD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	None	N/A
Keith A. Thompson, MD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	None	N/A
Jeffrey F. Patton, MD	Effective	Class I: Recommended	None	N/A
John M. Valgus, PharmD	Effective	Class I: Recommended	Existing trials closely indicate that Carbo is effective and may improve overall survival in this population.	N/A