TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Carboplatin

INDICATION: Testicular seminoma, stage 1, adjuvant, monotherapy

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
Oliver,R.T., et al: Radiotherapy versus single-dose carboplatin in adjuvant treatment of stage I seminoma: a randomised trial. Lancet Jul 23, 2005; Vol 366, Issue 9482; pp. 293-300.	Study methodology comments: This was a randomized, open-label, multicenter, noninferiority trial. Additional strengths of the study included: 1) defined primary and secondary outcomes; 2) conducted analyses on both the intent-to-treat and per-protocol populations; 3) had both inclusion and exclusion criteria; 4) compared baseline characteristics of treatment groups; 5) controlled the effect of potential confounding factors on treatment outcome; 6) confirmed diagnosis; 7) presented 95% confidence intervals; and 8) explained method of randomization. Weaknesses included 1) open-label design without the use of independent reviewers; and 2) possible selection bias since subjects were not recruited in a random or consecutive manner.	S
Oliver,R.T.D.: Randomized trial of carboplatin versus radiotherapy for stage I seminoma: Mature results on relapse and contralateral testis cancer rates in MRC TE19/EORTC 30982 study (ISRCTN27163214). Journal of Clinical Oncology Mar 10, 2011; Vol 29, Issue 8; pp. 957-962.	Study methodology comments: Updated results.	S
Aparicio,J., et al: Multicenter study evaluating a dual policy of postorchiectomy surveillance and selective adjuvant single-agent carboplatin for patients with clinical stage I seminoma. Ann Oncol Jun 2003; Vol 14, Issue 6; pp. 867-872.	Study methodology comments: This was an unrandomized trial that compared patients who received carboplatin with those who did not. Only patients considered at high risk of relapse received two courses of adjuvant carboplatin while patients at low risk underwent close surveillance. To account for the differences in risk between treatment groups, statistical analyses examined the effect of prognostic factors on outcomes. Additional strengths of the study included 1) had inclusion criteria; 2) confirmed diagnosis; and 3) presented 95% confidence intervals. Weaknesses included 1) absence of a power analysis; 2) open-label design without the use of independent reviewers; 3) did not present the results of most statistical analyses; and 4) possible selection bias since patients were not recruited in a random or consecutive manner.	S

Steiner,H., et al: Retrospective multicentre study of carboplatin monotherapy for clinical stage I seminoma. BJU Int Apr 2011; Vol 107, Issue 7; pp. 1074-1079.	Study methodology comments: This was a retrospective cohort study that should be interpreted with 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) did not present 95% confidence intervals; 3) absence of power analysis; 4) no exclusion criteria; and 5) did not examine the effect of potential confounding factors on outcomes. Strengths of the study included 1) had inclusion criteria; 2) confirmed diagnosis; and 3) reduced selection bias by enrolling consecutively presenting patients.	S
Dieckmann,K.P., et al: Adjuvant treatment of clinical stage I seminoma: is a single course of carboplatin sufficient?. Urology Jan 2000; Vol 55, Issue 1; pp. 102-106.	Study methodology comments: This was an open-label, time-series 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) absence of power analysis; and 3) possible selection bias since patients were not recruited in a random or consecutive manner. Strengths of the study included 1) had inclusion and exclusion criteria; 2) presented 95% confidence intervals; 3) assessed the effect of age on outcome; and 4) the use of a within-subject design to control for confounding effects of patient characteristics.	3
Reiter,W.J., et al: Twelve-year experience with two courses of adjuvant single-agent carboplatin therapy for clinical stage I seminoma. J Clin Oncol Jan 01, 2001; Vol 19, Issue 1; pp. 101-104.	Study methodology comments: This was an open-label, time-series 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) absence of power analysis; 3) did not present 95% confidence intervals; 4) did not examine the effect of potential confounding factors on outcomes; and 5) possible selection bias since patients were not recruited in a random or consecutive manner. Strengths included 1) had inclusion criteria; 2) confirmed diagnosis; and 3) the use of a within-subject design to control for confounding effects of patient characteristics.	3
Dieckmann,K.P., et al: Adjuvant carboplatin treatment for seminoma clinical stage I. Journal of Cancer Research and Clinical Oncology 1996; Vol 122, Issue 1; pp. 63-66.	Study methodology comments: This was an open-label, time-series 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) absence of power analysis; 3) did not present 95% confidence intervals; 4) did not examine the effect of potential confounding factors on outcomes; and 5) possible selection bias since patients were not recruited in a random or consecutive manner. Strengths included 1) had inclusion and exclusion criteria; and 2) the use of a within-subject design to control for confounding effects of patient characteristics.	3

Powles,T., et al: The long-term risks of adjuvant carboplatin treatment for stage I seminoma of the testis. Ann Oncol Mar 2008; Vol 19, Issue 3; pp. 443-447.	Study methodology comments: This was an observational study that should be interpreted with much caution. This study compared the data from the patients with age- and sex-matched general UK population data on mortality and incidence of second cancers. Weaknesses of the study included 1) wide confidence intervals; 2) no inclusion or exclusion criteria; 3) absence of a power analysis; 4) did not control for the effect of potential confounding factors on outcomes; 5) open-label design without the use of independent reviewers; and 6) possible selection bias since patients were not recruited in a random or consecutive manner. A strength of the study was that 95% confidence intervals were reported.	S
Aparicio,J., Germa,J.R., Garcia,del Muro,X, et al: Risk-adapted management for patients with clinical stage I seminoma: the Second Spanish Germ Cell Cancer Cooperative Group study. J Clin Oncol Dec 01, 2005; Vol 23, Issue 34; pp. 8717-8723.	Study methodology comments: This was an open-label, time-series trial that had two arms. Patients considered at high risk of relapse received two courses of adjuvant carboplatin while patients at low risk underwent close surveillance. This was not designed to be a comparative trial. Strengths of the study included 1) had inclusion and exclusion criteria; 2) confirmed diagnosis; 3) presented 95% confidence intervals; and 4) examined the effect of potential confounding factors on outcomes. Weaknesses included 1) absence of a power analysis; 2) open-label design without the use of independent reviewers; and 3) possible selection bias since patients were not recruited in a random or consecutive manner.	S
Pectasides,D., et al: Two cycles of carboplatin-based adjuvant chemotherapy for high-risk clinical stage I and stage IM non-seminomatous germ cell tumours of the testis: a HECOG trial. Anticancer Res Sep 2003; Vol 23, Issue 5b; pp. 4239-4244.		1
Krege,S., et al: Phase II study: adjuvant single-agent carboplatin therapy for clinical stage I seminoma. European Urology 1997; Vol 31, Issue 4; pp. 405-407.		3

Porcaro,AB., et al: Management of clinical stage I testicular pure seminoma. Report on 42 patients and review of the literature. Archivio Italiano di Urologia, Andrologia - Organo Ufficiale di Societa Italiana di Ecografia Urologica e Nefrologica / Associazione Ricerche in Urologia Jun 2002; Vol 74, Issue 2; pp. 77-80.		1
Krege,S., et al: Single agent carboplatin for CS IIA/B testicular seminoma. A phase II study of the German Testicular Cancer Study Group (GTCSG). Ann Oncol Feb 2006; Vol 17, Issue 2; pp. 276-280.		1
Patterson,H.: Combination carboplatin and radiotherapy in the management of stage II testicular seminoma: Comparison with radiotherapy treatment alone. Radiotherapy and Oncology Apr 01, 2001; Vol 59, Issue 1; pp. 5-11.		1
Kratzik,C., Reiter,W.J., and Schrey,A.: 10 Years experience with adjuvant single-agent carboplatin therapy for clinical stage I seminoma. Journal of Urology Apr 1999; Vol 161, Issue 4 SUPPL.; p. 181.	Study methodology comments: Abstract	3
Steiner,H., et al: Very Low Recurrence Rate After Long Experience with Adjuvant Carboplatin Montherapy for Clinical Stage I Seminoma. Journal of Urology Apr 2009; Vol 181, Issue N4,S; pp. 325-325.	Study methodology comments: Abstract	3

Decatris,M.P. and Kitsios,P.: Updated Results of Adjuvant Carboplatin (Carbo Auc 7 and 7.7) in Stage I Seminoma (Sem) of the Testis from the Boc Oncology Centre. Annals of Oncology Jan 2010; Vol 21, Issue 8; pp. 294-294.	Study methodology comments: Abstract	3
Faris,M., et al: Evaluation of the role of a single cycle of carboplatin as an adjuvant treatment in stage I seminoma and as a neo-adjuvant prior to radiotherapy in stage II. European Journal of Cancer Sep 1997; Vol 33, Issue 8; pp. 182-182.	Study methodology comments: Abstract	3
Oliver,R.T., et al: A randomised comparison of single agent carboplatin with radiotherapy in the adjuvant treatment of stage I seminoma of the testis, following orchidectomy: MRC TE19/EORTC 30982. Journal of Clinical Oncology Jul 15, 2004; Vol 22, Issue N14,S; pp. 386S-386S.	Study methodology comments: Abstract	3
Oliver,T., et al: Pooled analysis of phase 2 reports of 2 v 1 course of carboplatin as adjuvant for stage 1 seminoma. Journal of Clinical Oncology Jun 01, 2005; Vol 23, Issue N16,1,S; pp. 395S-395S.	Study methodology comments: Abstract	3
Decatris MP, Kitsios P. Single-agen carboplatin for stage I seminoma of the testis: A single institution experience. 33rd ESMO Congress, Stockholm 2008 Poster.		3

Chung,P.: Radiotherapy versus single-dose carboplatin in adjuvant treatment of stage I seminoma: A commentary. American Journal of Oncology Review Jan 01, 2006; Vol 5, Issue 1; pp. 29-30.		4
Aparicio,Jorge and Diaz,Roberto: Management options for stage I seminoma. Expert Review of Anticancer Therapy Jul 2010; Vol 10, Issue 7; pp. 1077-1085.		4
Classen,J., et al: Treatment of early stage testicular seminoma. Journal of Cancer Research and Clinical Oncology Aug 2001; Vol 127, Issue 8; pp. 475-481.		4
Huddart,R.A.: Testicular seminoma: ESMO Clinical Recommendations for diagnosis, treatment and follow-up ESMO Clinical Recommendations. Annals of Oncology May 01, 2007; Vol 18, Issue SUPPL. 2; pp. ii40-ii41.		4
Warde,P. and Gospodarowicz,M.: Adjuvant carboplatin in stage I seminoma. Lancet Jul 23, 2005; Vol 366, Issue 9482; pp. 267-268.		4
Chung,P.: Management of Stage I Seminomatous Testicular Cancer: a Systematic Review. Clinical Oncology Feb 01, 2010; Vol 22, Issue 1; pp. 6-16.		4

Bosl,g.J. and Patil,S.: Carboplatin in clinical stage I seminoma: too much and too little at the same time. J Clin Oncol Mar 10, 2011; Vol 29, Issue 8; pp. 949-952.		4
Martin,J.M., et al: Evidence-based guidelines for following stage 1 seminoma. Cancer Jun 01, 2007; Vol 109, Issue 11; pp. 2248-2256.		4
Rowland,R.G.: Radiotherapy versus single-dose carboplatin in adjuvant treatment of stage I seminoma: A randomised trial - Commentary. Urologic Oncology: Seminars and Original Investigations Mar 01, 2006; Vol 24, Issue 2 SPEC. ISS.; p. 175.		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
Margi Schiefelbein, PA	None	Edward Balaban, DO	None
Stacy LaClaire, PharmD	None	James Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffery F. Patton, MD	None
		Keith Thompson, MD	None
		John Valgus, PharmD	None

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward Balaban, DO	Effective	Class IIa: Recommended, In Most Cases	Borders on class 1 recommendation rating	N/A
James Liebmann, MD	Effective	Class IIb: Recommended, In Some Cases	Carboplatin, at an AUC=7 for 1 or 2 cycles, is one of three rational options for stage 1a or 1b seminoma. Which option (carboplatin, surveillance, or radiation) will depend on patient preference and other factors. Note that the NCCN guidelines also identify carboplatin as a category 1 option for this disease	N/A
Jeffery F. Patton, MD	Effective	Class IIb: Recommended, In Some Cases	Active observation remains a reasonable option	N/A
Keith Thompson, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	N/A

John Valgus, PharmD	Effective	Class IIa: Recommended, In Most Cases	Randomized trial with long term FU clearly demonstrates efficacy. Safety also demonstrated. Only one randomized trial available so only rec, in most cases.	N/A