TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Carboplatin

INDICATION: Metastatic breast cancer, HER2 overexpression, first-line therapy in combination with a taxane and trastuzumab

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, 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
Valero V, et al. Multicenter phase III randomized trial comparing docetaxel and trastuzumab with docetaxel, carboplatin, and trastuzumab as first-line chemotherapy for patients with HER2-gene-amplified metastatic breast cancer (BCIRG 007 study): two highly active therapeutic regimens. J Clin Oncol. 2011 Jan 10;29(2):149-56. Epub 2010 Nov 29.	Study methodology comments: This was an open-label, randomized, comparative trial. Additional strengths of the study included 1) had both inclusion and exclusion criteria; 2) controlled for the effect of many confounding factors on outcomes; 3) defined response; 4) defined primary and secondary endpoints; 5) conducted a power analysis; 6) compared baseline characteristics of groups; 7) presented 95% confidence intervals; 8) confirmed responses at 4 weeks; and 9) explained method of randomization. Weaknesses included 1) open-label design without the use of independent reviewers; and 2) possible selection bias since patients were not recruited in a random or consecutive manner.	S
Robert,N., et al: Randomized phase III study of trastuzumab, paclitaxel, and carboplatin compared with trastuzumab and paclitaxel in women with HER-2-overexpressing metastatic breast cancer. J Clin Oncol Jun 20, 2006; Vol 24, Issue 18; pp. 2786-2792.	Study methodology comments: This was an open-label, randomized, comparative trial. Additional strengths of the study included 1) had both inclusion and exclusion criteria; 2) controlled for the effect of some confounding factors on outcomes; 3) defined response; 4) defined primary and secondary objectives; 5) conducted a power analysis; 6) compared baseline characteristics of groups; 7) presented 95% confidence intervals; 8) responses were confirmed at 4 weeks; and 9) confirmed diagnosis. Weaknesses included 1) open-label design without the use of independent reviewers; 2) no explanation of the method of randomization; and 3) possible selection bias since patients were not recruited in a random or consecutive manner.	S
Fountzilas,G., et al: A randomized phase III study comparing three anthracycline-free taxane-based regimens, as first line chemotherapy, in metastatic breast cancer: a Hellenic Cooperative Oncology Group study. Breast Cancer Research and Treatment May 2009; Vol 115, Issue 1; pp. 87-99	Study methodology comments: This was an open-label, randomized, comparative trial. Additional strengths of the study included 1) had both inclusion and exclusion criteria; 2) controlled for the effect of many confounding factors on outcomes; 3) defined response; 4) defined primary and secondary objectives; 5) conducted a power analysis; 6) compared baseline characteristics of groups; 7) presented 95% confidence intervals; and 8) confirmed diagnosis. Weaknesses included 1) open-label design without the use of independent reviewers; 2) partial explanation of the method of randomization; and 3) possible selection bias since patients were not recruited in a random or consecutive manner. Clinical comments: Only about 30% of patients were HER2+ and received Trastuzumab. Results not stratified.	3

Perez,Edith A., et al: Two concurrent phase II trials of paclitaxel/carboplatin/trastuzumab (weekly or every-3-week schedule) as first-line therapy in women with HER2-overexpressing metastatic breast cancer: NCCTG study 983252. Clinical Breast Cancer Dec 2005; Vol 6, Issue 5; pp. 425-432.		3
Burris,H.,III, et al: Phase II trial of trastuzumab followed by weekly paclitaxel/carboplatin as first-line treatment for patients with metastatic breast cancer. J Clin Oncol May 01, 2004; Vol 22, Issue 9; pp. 1621-1629.		3
Ruiz,M., et al: Phase-II study of weekly schedule of trastuzumab, paclitaxel, and carboplatin followed by a week off every 28 days for HER2+ metastatic breast cancer. Cancer Chemotherapy and Pharmacology Nov 2008; Vol 62, Issue 6; pp. 1085-1090		3
Perez,E.A., et al: N98-32-52: Efficacy and tolerability of two schedules of paclitaxel, carboplatin and trastuzumab in women with HER2 positive metastatic breast cancer: A North Central Cancer Treatment Group randomized phase II Trial. Breast Cancer Research and Treatment 2003; Vol 82, Issue Supplement 1; p. S47.		3
Cardoso,F.: Locally recurrent or metastatic breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology May 01, 2010; Vol 21, Issue SUPPL. 5; pp. v15-v19.		4

Dirix,L., et al: Phase II study of Docetaxel, Carboplatin, and Trastuzumab (THC) as first-line treatment in patients with HER-2 amplified advanced breast cancer. Changes in circulating tumor cells (CTC), total plasma DNA and Circulating HER-2 ECD. EJC Supplements Mar 2006; Vol 4, Issue 2; p. 161.		3
Pegram,M.D., et al: Results of two open-label, multicenter phase II studies of docetaxel, platinum salts, and trastuzumab in HER2-positive advanced breast cancer. J Natl Cancer Inst May 19, 2004; Vol 96, Issue 10; pp. 759-769.		2
Perez,E.A.: Carboplatin in combination therapy for metastatic breast cancer. The Oncologist 2004; Vol 9, Issue 5; pp. 518-527		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 P. Balaban, DO	None
Stacy LaClaire, PharmD	None	Thomas McNeil Beck, MD	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
Edward P. Balaban, DO	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	Difficult since the data shown is in HER2 (+) only. However, other data would suggest (if not more than suggest) efficacy in other subsets of breast ca.	N/A
Thomas McNeil Beck, MD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	Reports variable -	N/A
James E. Liebmann, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	Platinum analogues were shown to be active agents in breast cancer 25 years ago. TCH or TPC are clearly effective regimens with acceptable response rates as well as reasonable PFS and OS rates. For patients who cannot tolerate anthracyclines, the regimens are particularly attractive. However, doubt remains whether (Carboplatin and Taxane) is better than (Taxane) alone. For that reason, it is not possible to give the combination a “Class IIa” rating.	N/A

Keith A. Thompson, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	N/A
John M. Valgus, PharmD	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Acceptable regimen in combination with paclitaxel only. Currently listed as preferred regimen in NCCN. Superior PFS with paclitaxel.	N/A