COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 3/14/16

PACKET: 1283

DRUG: Carboplatin

USE: Triple negative breast cancer, neoadjuvant, in combination with chemotherapy

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
Von Minckwitz G et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol 2014; 15: 747–56.	Comments: This was a multi-site, randomized trial. Key bias criteria evaluated were (1) random sequence generation of randomization; (2) lack of allocation concealment, (3) lack of blinding, (4) incomplete accounting of patients and outcome events, and (5) selective outcome reporting bias. The study was at low risk of bias for these key criteria, and no additional biases were identified.	S
Sikov WM et al. Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance). J Clin Oncol 33:13-21.	Comments: This was open-label, randomized trial. Overall, this study was at low risk for most of the key risk of bias criteria which included lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of biases associated with random sequence generation and allocation concealment were unclear and not discussed in the paper.	S
Ando M, et al. Randomized phase II study of weekly paclitaxel with and without carboplatin followed by cyclophosphamide/ epirubicin/5-fluorouracil as neoadjuvant chemotherapy for stage II/IIIA breast cancer without HER2 overexpression. Breast Cancer Res Treat (2014) 145:401–409	Comments: This was a multi-site, open-label, randomized trial. Overall, this study was at low risk for most of the key risk of bias criteria which included random sequence generation, lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with allocation concealment was unclear and not discussed in the paper.	S

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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		Jeffrey Klein	None
		John D Roberts	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, nonrandomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12 month period and observed for 36 months.

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases		A
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	The addition of Carboplatin in these studies showed a substantial benefit to the patient with regard to improving pathological response rates over those patients who were not given the carboplatin "arm". However the benefits gained came with a "price". Significant hematological toxicities such as neutropenia and thrombocytopenia occurred. Non-hematological adverse effects resulted as well. Patients and their oncologists must truly evaluate if the benefits of the product outweigh its risks. It also seems that patients had to drop out of the studies due to these harmful effects. One must also consider that these tested patients were stage II and III TNBC only. Also must be questioned if there are more "advanced" agents on the market that can have the same benefits with less toxicity?	N/A

John D Roberts	Evidence is Inconclusive	Class lll: Not Recommended	Evidence to date suggests that addition of carboplatin to some standard neo-adjuvant chemotherapy regimens may improve complete response rates and probably increases toxicity. There is uncertainty about the optimal dose in terms of response versus toxicity. Historically, pathological complete response may or may not predict for progression free and/or overall survival benefit. Thus, carboplatin should not be recommended outside of a clinical trial.	N/A
Richard LoCicero	Evidence Favors Efficacy	Class llb: Recommended, In Some Cases	In the neoadjuvant setting, the addition of carboplatin to chemotherapy regimens has been associated with improved pathologic complete remission (pCR) rates. In general, improved pCR is associated with better outcomes. However, the carboplatin trials have not established improvements in overall survival or disease free survival.	N/A