TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: **JUNE 2015**

PACKET: **1221**

DRUG: **Exemestane**

INDICATION: **Breast cancer, adjuvant, premenopausal, in combination with ovarian suppression**

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, L *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
Pagani O et al. Adjuvant Exemestane with Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med 2014;371:107-18.	Study methodology comments: Overall, this study has a crucial limitation for one criterion sufficient to lower ones confidence in the estimate effect. There was potentially high bias for lack of blinding since this was an open-label trial that did not use independent reviewers or assessors. There was low risk of bias associated with incomplete accounting of patients and outcome events, selective outcome reporting, allocation concealment, and random sequence generation.	S
Francis,P.A., Regan,M.M., Fleming,G.F., et al: Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med Dec 11, 2014; Vol E Pub, p. 1.	Study methodology comments: Overall, this study has a crucial limitation for one criterion sufficient to lower ones confidence in the estimate effect. There was potentially high bias for lack of blinding since this was an open-label trial that did not use independent reviewers or assessors. There was low risk of bias associated with incomplete accounting of patients and outcome events, selective outcome reporting, allocation concealment, and random sequence generation.	2
Olivia Pagani et al. Randomized comparison of adjuvant aromatase inhibitor (AI) exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Joint analysis of IBCSG TEXT and SOFT trials. Journal of Clinical Oncology, 2014 ASCO Annual Meeting Abstracts. Vol 32, No 18_suppl (June 20 Supplement), 2014	Study methodology comments: Abstract	4

Chlebowski,R.T. and Pan,K.: Exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med Oct 02, 2014; Vol 371, Issue 14; p. 1358.		4
Pagani,O., Regan,M.M., and Francis,P.A.: Exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med Oct 02, 2014; Vol 371, Issue 14; pp. 1358-1359		2

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	Edward Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffrey A. Bubis, DO	Other payments: Dendreon
		Jeffrey Patton, MD	None
		Keith Thompson, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward Balaban, DO	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	With the current trial Exemestane plus ovarian suppression appears equal to Tamoxifen and ovarian suppression in premenopausal females. Really struggle to make it superior. Also there is a Tamoxifen alone ARM still pending. In summary could easily be considered IIa strength.	N/A

James E. Liebmann, MD	Effective	Class IIb: Recommended, In Some Cases	The reviewed trial, together with data from use of aromatase inhibitors in postmenopausal women as well as publication of the SOFT Tamoxifen data permit some reasonable conclusions. First, ovarian suppression (OS) plus exemestane more effectively prevents breast cancer recurrence than either tamoxifen alone or tamoxifen with OS in premenopausal women. Second, the greatest absolute benefit from OS is likely found in women who receive chemotherapy but who do not enter menopause as a result of chemotherapy. Third, OS plus exemestane is more toxic than tamoxifen or tamoxifen and OS in premenopausal women, leading to higher rates of discontinuation of treatment. Fourth, there is as yet no evidence that OS plus exemestane results in better long term survival for premenopausal women with early stage breast cancer compared to tamoxifen or tamoxifen plus OS. Therefore, exemestane with OS is a very reasonable option for premenopausal women with breast cancer, though I imagine it will be reserved for women at greatest risk of relapse.	N/A
Jeffrey A. Bubis, DO	Ineffective	Class III: Not recommended	This is more costly than tamoxifen, but no more effective in overall survival.	N/A
Jeffrey Patton, MD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	None	
Keith Thompson, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	