TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 10/24/2018

PACKET: 1796

DRUG: Tamoxifen

USE: Malignant tumor of breast, adjuvant therapy, premenopausal, hormone receptor-positive, 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: C, E, 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
Francis,P.A., et al: Tailoring adjuvant endocrine therapy for premenopausal breast cancer. N Engl J Med Jul 12, 2018; Vol 379, Issue 2; pp. 122-137.		S
Ribi,K., et al: Adjuvant tamoxifen plus ovarian function suppression versus tamoxifen alone in premenopausal women with early breast cancer: patient-reported outcomes in the Suppression of Ovarian Function Trial. J Clin Oncol May 10, 2016; Vol 34, Issue 14; pp. 1601-1610.	SOFT Trial comments: This study is a multi-national, phase 3, randomized trial designed to evaluate five years of tamoxifen versus a combination of five years of tamoxifen plus ovarian function suppression (OFS) versus a combination of five years of exemestane plus OFS. 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. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors. TEXT Trial comments: This study is a multi-national, phase 3, randomized trial designed to evaluate five years of tamoxifen versus a combination of five years of tamoxifen plus ovarian function suppression (OFS) versus a combination of five years of exemestane plus OFS. 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. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	S

Burstein,H.J., et al: Adjuvant Endocrine Therapy for Women With Hormone Receptor-Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update on Ovarian Suppression. J Clin Oncol Feb 16, 2016;		S
Saha,P., et al: Treatment Efficacy, Adherence, and Quality of Life Among Women Younger Than 35 Years in the International Breast Cancer Study Group TEXT and SOFT Adjuvant Endocrine Therapy Trials. J Clin Oncol Sep 20, 2017; Vol 35, Issue 27; pp. 3113-3122.		3
Yan,S., et al: Tamoxifen with ovarian function suppression versus tamoxifen alone as an adjuvant treatment for premenopausal breast cancer: a meta-analysis of published randomized controlled trials. Onco.Targets Ther 2015; Vol 8, pp. 1433-1441.	Comments: This was a systematic review which included four randomized phase 3 trials comprising 6,279 patients (OFS combination, n=3,133; tamoxifen alone, n=3,146). The risk of bias tool was used to assess the quality of the included trials. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	3
Gori,S.: Adjuvant endocrine therapy in premenopausal patients with hormone receptor-positive early breast cancer: Evidence evaluation and GRADE recommendations by the Italian Association of Medical Oncology (AIOM). Eur J Cancer Aug 01, 2018; Vol 99, pp. 9-19.		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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, 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 is Inconclusive	Class III: Not Recommended		B
John D Roberts	Evidence is Inconclusive	Class III: Not Recommended	Albeit not yet mature, overall survival data do not show a benefit of adding ovarian suppression to tamoxifen, but an increase in toxicity is clear. Post-hoc analyses suggest that certain subgroups may benefit, but the differences are small and cannot be relied upon. Uncertainty is underscored by contrary findings in comparisons of tamoxifen and exemustine without and with ovarian suppression in multiple analyses of endpoints other than overall survival.	N/A
Jeffrey Klein	Ineffective	Class III: Not Recommended	The addition of ovarian suppression to Tamoxifen did not have any significant benefit to prevent breast cancer reoccurance, the data from the trials provided clearly support this. If used alone Tamoxifen showed a good degree of benefit to warrant its use.	N/A

Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Adjuvant endocrine therapy (such as Tamoxifen) is a well established treatment for the adjuvant management of ER/PR+ breast cancer. Clinical trials have established ovarian suppression in addition to Tamoxifen is superior to Tamoxifen therapy alone. This approach is most effective in patients who also received adjuvant chemotherapy. While aromatase inhibitor therapy (in combination with ovarian suppression) is more effective than Tamoxifen in this setting, some patients may prefer Tamoxifen due to toxicity or other factors. To emphasize, conflicting clinical trial data exists to support the use of Tamoxifen in combination with ovarian suppression. Evidence-based, concensus guidelines continue to support its use based on clinical factors and patient choice.	N/A