TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Triptorelin pamoate

INDICATION: Post-chemotherapy ovarian failure, in premenopausal women with breast cancer, prophylaxis

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**
*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
Alison W. Loren, et al. 2013 Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update.		S
Del,Mastro L., et al: Effect of the gonadotropin-releasing hormone analogue triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer: a randomized trial. JAMA Jul 20, 2011; Vol 306, Issue 3; pp. 269-276.	Study methodology comments: This was a randomized, open-label, phase III trial. Overall, this study was at low risk for most of the key risk of bias criteria which included lack of allocation concealment, lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation was unclear and not discussed in the paper.	S
Eman A. Elgindy, et al. Gonadatrophin Suppression to Prevent Chemotherapy-Induced Ovarian Damage - A Randomized Controlled Trial. Obstet Gynecol 2013;121:78–86.	Study methodology comments: This was a two-center, four-armed, open-label 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
Munster,P.N., et al: Randomized trial using gonadotropin-releasing hormone agonist triptorelin for the preservation of ovarian function during (neo)adjuvant chemotherapy for breast cancer. J Clin Oncol Feb 10, 2012; Vol 30, Issue 5; pp. 533-538.	Study methodology comments: This was a randomized, open-label trial. The study had originally planned to enroll a total of 124 patients with an expected amenorrhea rate of 10% in the triptorelin arm, based on historical data, and 30%in the control arm. However, the observed amenorrhea rate in this randomized, age- and regimen-stratified study was comparable in both arms (10% and 12%). Overall, this study was at low risk of bias 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
Celio,L., et al: Premenopausal breast cancer patients treated with a gonadotropin-releasing hormone analog alone or in combination with an aromatase inhibitor: A comparative endocrine study. Anticancer Research 1999; Vol 19, Issue 3 B; pp. 2261-2268.	Study methodology comments: This was a randomized, single-blind trial. Overall, this study was at low risk of bias 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 bias associated with lack of random sequence generation and allocation concealment was unclear and not discussed in the paper.	1

Yang,B., Shi,W., Yang,J., et al: Concurrent treatment with gonadotropin-releasing hormone agonists for chemotherapy-induced ovarian damage in premenopausal women with breast cancer: A meta-analysis of randomized controlled trials. Breast Apr 2013; Vol 22, Issue 2; pp. 150-157.		4
Blumenfeld,Z.: Preservation of ovarian function and minimizing premature ovarian failure during chemotherapy using gonadotropin-releasing hormone analogs. Women's Health Nov 2011; Vol 7, Issue 6; pp. 635-640.		4
Turner,N.H., Partridge,A., Sanna,G., et al: Utility of gonadotropin-releasing hormone agonists for fertility preservation in young breast cancer patients: The benefit remains uncertain. Annals of Oncology 2013; Vol 24, Issue 9; pp. 2224-2235.		4
Mersereau,J.E. and Sandbulte,J.T.: Fertility Preservation in Young Women with Breast Cancer. Current Obstetrics and Gynecology Reports 2013; Vol 2, Issue 1; pp. 59-64.		4
Rugo,H.S. and Rosen,M.P.: Reducing the long-term effects of chemotherapy in young women with early-stage breast cancer. JAMA - Journal of the American Medical Association Jul 20, 2011; Vol 306, Issue 3; pp. 312-314.		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

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	Thomas A. Marsland, MD	None
		Jeffrey F. Patton, MD	None
		James E. Liebmann, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		A
Edward P. Balaban, DO	Evidence is inconclusive	Class III - Not Recommended	Data too conflicting to justify using as prophylaxis.	N/A
Thomas McNeil Beck, MD	Ineffective	Class III - Not Recommended	No significant protection of ovarian function.	N/A
Thomas A. Marsland, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	Literature is contradictory. No true conclusions can be obtained. Interesting the role of ovarian suppression as treatment is not addressed. Literature now recommends 10 years of tamoxifen - one of the studies reviewed actually reinstituted ovarian blockade if the patient did resume menses	N/A
Jeffrey F. Patton, MD	Evidence is inconclusive	Class III - Not Recommended	None	N/A

James E. Liebmann, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	Trials of ovarian suppression during chemotherapy in women with breast cancer have resulted in conflicting results. While the data in the Del Mastro et al study are encouraging, other studies, including some in the current packet, do not show a reduction in risk of ovarian failure with the use of GnRHa during chemotherapy. Accordingly, I must agree with the ASCO guidelines that GnRHa should be used only in "rare or extreme circumstances" when other options for preservation of fertility are not available.	N/A