

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: APRIL 2015
PACKET: 997
DRUG: Zoledronic acid
INDICATION: Breast cancer, early stage, adjuvant

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 *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)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Valachis,A, Polyzos,NP, Coleman,RE, et al: Adjuvant therapy with zoledronic acid in patients with breast cancer: a systematic review and meta-analysis. Oncologist 2013; Vol 18, Issue 4; pp. 353-361.	This was a systematic review/meta-analysis that included 15 randomized-controlled trials. The authors used the Risk of Bias tool to assess the quality of the included trials. The analyses showed low to moderate heterogeneity (I^2 ranged from 0% to 55%).	S
He,M., Fan,W., and Zhang,X.: Adjuvant zoledronic acid therapy for patients with early stage breast cancer: an updated systematic review and meta-analysis. J Hematol Oncol 2013; Vol 6, Issue 1; p. 80.		2
Ben-Aharon,I., Vidal,L., Rizel,S., et al: Bisphosphonates in the Adjuvant Setting of Breast Cancer Therapy-Effect on Survival: A Systematic Review and Meta-Analysis. PLoS ONE [Electronic Resource] Aug 2013; Vol 8, p. 1.		2
Van Poznak,C.: The efficacy of zoledronic acid in breast cancer adjuvant therapy: A meta-analysis of randomised controlled trials. Breast Diseases 2013; Vol 24, Issue 1; pp. 68-70.		2

<p>Ahn,S.G., Kim,S.H., Lee,H.M., et al: Survival benefit of zoledronic acid in postmenopausal breast cancer patients receiving aromatase inhibitors. Journal of Breast Cancer Dec 2014; Vol 17, Issue 4; pp. 350- 355.</p>		<p>3</p>
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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	Jeffrey A. Bubis, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Edward Balaban, DO	None
		Thomas Marsland, MD	None
		Jeffrey Patton, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Jeffrey A. Bubis, DO	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	It is unclear as to whether this is related to disease or not as DFS didn't change (though OS did). The risk:benefit ratio remains unclear, but should be considered in patients with bone loss.	N/A

James E. Liebmann, MD	Evidence is Inconclusive	Class III: Not Recommended	The meta-analysis cited as justification for the use of zolderonic acid (ZA) as adjuvant therapy for early stage breast cancer can be considered hypothesis-generating, but not a definitive validation. Note that the single largest trial cited in the meta-analysis, the AZURE trial which comprised over 40% of the patients analyzed in this review, was a negative trial. The authors of the AZURE trial concluded, "...our findings do not support the routine use of zoledronic acid as adjuvant therapy in unselected patients with early-stage breast cancer." (NEJM 365;1396, 2011). The authors of the current meta-analysis cite another meta-analysis (Yan, et al) that concluded that ZA did not provide benefit to women with early stage breast cancer. At present, the use of bisphosphonates as adjuvant therapy of early stage breast cancer remains a subject for clinical trials.	N/A
Edward Balaban, DO	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	In spite of meta-analyses, I'm not convinced zoledronic acid has a role in the adjuvant setting. Many studies done, but results are not impressive or convincing. If it appears to have any role, it might be in the post-menopausal female only. Class IIb at most.	N/A

Thomas Marsland, MD	Evidence Favors Efficacy	Class I: Recommended	Multiple studies and meta analysis of randomized study suggest statistically significant improvement in OS and decrease in fracture with good safety profile. As aside, was just at ASCO annual meeting where additional positive studies were presented. The drug should be used.	N/A
Jeffrey Patton, MD	Effective	Class IIa: Recommended, In Most Cases	None	N/A