COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 2/2/16

PACKET: 1257

DRUG: Arsenic Trioxide

USE: Acute promyelocytic leukemia, FAB M3 newly diagnosed, low to intermediate risk, in combination with all-trans retinoic acid

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, 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)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Lo-Coco et al. Retinoic Acid and Arsenic Trioxide for Acute Promyelocytic Leukemia. N Engl J Med 2013;369:111-21.	Comments: This was a randomized, multicenter, open-label, phase 3 noninferiority trial. Overall, this study was at low risk of biases associated with lack of allocation concealment and blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation was unclear.	S
Burnett et al. Arsenic trioxide and all-trans retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomised, controlled, phase 3 trial. Lancet Oncol 2015; 16: 1295–1305.		2
Powell et al. Arsenic trioxide improves eventfree and overall survival for adults with acute promyelocytic leukemia: North American Leukemia Intergroup Study C9710. Blood. 2010 Nov 11; 116(19): 3751–3757.		1
Ma,H. and Yang,J.: Insights into the all-trans-retinoic acid and arsenic trioxide combination treatment for acute promyelocytic leukemia: a meta-analysis. Acta Haematologica Jul 25, 2015; Vol 134, Issue 2; pp. 101-108.		1

Chen,L., Wang,J., Hu,X., et al: Meta-analysis of all-trans retinoic acid-linked arsenic trioxide treatment for acute promyelocytic leukemia. Hematology Jun 2014; Vol 19, Issue 4; pp. 202-207.		1
Wang,H., Chen,X.-Y., Wang,B.-S., et al: The efficacy and safety of arsenic trioxide with or without all-trans retinoic acid for the treatment of acute promyelocytic leukemia: A meta-analysis. Leukemia Research Sep 2011; Vol 35, Issue 9; pp. 1170-1177.		1
Lo-Coco,F., Tallman,M.S., Barnes,G., et al: A meta-analysis of randomized clinical trials in acute promyelocytic leukemia (APL). Journal of Clinical Oncology 2015; Vol 33, Issue 15 SUPPL. 1; p. 7040.	Abstract	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 article, letter, commentary, or editorial)

CONTRIBUTORS:
*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Felicia Gelsey, MS	None	Robert LoCicero	None
Stacy LaClaire, PharmD	None	John D Roberts	None
Catherine Sabatos, PharmD	None	Mark Levin	None

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Effective	Class IIa: Recommended, In Most Cases		B
Robert LoCicero	Effective	Class I: Recommended	The Lo-Coco trial established that arsenic trioxide in combination with all-trans retinoic acid is an effective combination (at least as effective as the current standard) in a randomized, multicenter, phase III trial. Additionally, this combination is a category I recommendation supported by the National Comprehensive Cancer Network.	N/A
John D Roberts	Effective	Class IIa: Recommended, In Most Cases	Lo-Coco et al NEJM 2013 show arsenic trioxide to be as or more effective than a standard chemotherapy regimen in combination with all trans retinoic acid for the treatment of low or intermediate risk acute promyelocytic leukemia. Side effect profiles of the two regimens are different with, for example, more liver toxicity in the arsenic trioxide regimen. Thus, this regimen might not be appropriate for patients with pre-existing liver disease.	N/A

Mark Levin	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	The drug si celarly effective but restricted to only one and fairly uincommon typoe of AML, which is why I selected IIb. In the cases of APL with the appropriate mutation (see below)approved, the drug is appropriate and FDA indicated. TRISENOX is indicated for induction of remission and consolidation in patients with acute promyelocytic leukemia (APL) who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation orPML/RAR-alpha gene expression.	N/A