COMPENDIA TRANSPARENCY TRACKING FORM

DATE: September 21, 2023

OFF-LABEL ID #: 2619

DRUG NAME: Enasidenib

OFF-LABEL USE: Acute myeloid leukemia, disease Newly diagnosed, IDH2 mutation positive, monotherapy or in combination with azacitidine; in patients ineligible for intensive chemotherapy

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, L, 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	LITERATURE CODE
DiNardo CD, Schuh AC, Stein EM, et al. Enasidenib plus azacitidine versus azacitidine alone in patients with newly diagnosed, mutant-IDH2 acute myeloid leukaemia (AG221-AML-005): a single-arm, phase 1b and randomised, phase 2 trial. Lancet Oncol. 2021 Nov;22(11):1597-1608. doi: 10.1016/S1470-2045(21)00494-0. Epub 2021 Oct 18. PMID: 34672961.	S
Pollyea DA, Tallman MS, de Botton S, et al. Enasidenib, an inhibitor of mutant IDH2 proteins, induces durable remissions in older patients with newly diagnosed acute myeloid leukemia. Leukemia. 2019 Nov;33(11):2575-2584. doi: 10.1038/s41375-019-0472-2. Epub 2019 Apr 9. PMID: 30967620; PMCID: PMC9724489.	S
Wang L, Song J, Xiao X, et al. Comparison of venetoclax and ivosidenib/enasidenib for unfit newly diagnosed patients with acute myeloid leukemia and *IDH1/2* mutation: a network meta-analysis. J Chemother. 2023 Aug 20:1-6. doi: 10.1080/1120009X.2023.2247200. Epub ahead of print. PMID: 37599456.	3
Stein EM, DiNardo CD, Fathi AT, et al. Ivosidenib or enasidenib combined with intensive chemotherapy in patients with newly diagnosed AML: a phase 1 study. Blood. 2021 Apr 1;137(13):1792-1803. doi: 10.1182/blood.2020007233. PMID: 33024987; PMCID: PMC8020270.	1

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
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
MERATIVE MICROMEDEX	Effective	Class IIa: Recommended, in Most Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Enasidenib alone or in combinatiion with azacitidine demonstrated a good overall response rate in newly diagnosed AML patients who are IDG2 mutation positive. The degree of serious adverse effects with Enasidenib needs to be considered though.	
Richard LoCicero	Effective	Class IIa: Recommended, in Most Cases	In two phase I/II trials, enasidenib efficacy was demonstrated in patients ineligible for intensive chemotherapy with IDH2 mutation positive acute myeloid leukemia. Complete remissions were achieved in 18% (monotherapy) and 54% (in combination with azacitadine). No unexpected toxicity was observed.	

Todd Gersten	Effective	Class I: Recommended	Enasidenib has demonstrated a high degree of efficacy/responses and durable responses when used as monotherapy or in combination with azacitadine in untreated AML with IDH2 mutations cases unsuitable for intensive treatment.	