merative

Micromedex

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: July 13, 2022

OFF-LABEL ID #: 2419

DRUG NAME: Venetoclax

OFF-LABEL USE: Myelodysplastic syndrome (clinical); In combination with azacitidine or decitabine

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, *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
Khanam R, Shahzad M, Chaudhary SG, et al. Outcomes after venetoclax with hypomethylating agents in myelodysplastic syndromes: a systematic review and meta-analysis. Leuk Lymphoma. 2022 Jun 10:1-8.	This was a systematic review and meta-analysis that included sixteen prospective and retrospective single-arm studies of 393 patients with MDS. The authors used the Before-After studies tool published by the National Institutes of Health to measure the quality of the included studies, and all studies were deemed of "good" quality. The analyses showed low to moderate heterogeneity, and the appropriate statistical models were used.	S
Lachowiez CA, Reville PK, Kantarjian Het al. Venetoclax combined with induction chemotherapy in patients with newly diagnosed acute myeloid leukaemia: a post-hoc, propensity score-matched, cohort study. Lancet Haematol. 2022 May;9(5):e350-e360.		1
Kadia TM, Reville PK, Borthakur G, et al. Venetoclax plus intensive chemotherapy with cladribine, idarubicin, and cytarabine in patients with newly diagnosed acute myeloid leukaemia or high-risk myelodysplastic syndrome: a cohort from a single-centre, single-arm, phase 2 trial. Lancet Haematol. 2021 Aug;8(8):e552-e561.		1
Garcia JS, Kim HT, Murdock HM, et al. Adding venetoclax to fludarabine/busulfan RIC transplant for high-risk MDS and AML is feasible, safe, and active. Blood Adv. 2021 Dec 28;5(24):5536-5545.		2

Wei Y, Xiong X, Li X, Lu W, He X, Jin X, Sun R, Lyu H, Yuan T, Sun T, Zhao M. Low-dose decitabine plus venetoclax is safe and effective as post-transplant maintenance therapy for high-risk acute myeloid leukemia and myelodysplastic syndrome. Cancer Sci. 2021 Sep;112(9):3636-3644. doi: 10.1111/cas.15048. Epub 2021 Jul 21. PMID: 34185931; PMCID: PMC8409404.		1
Feld J, Tremblay D, Dougherty M, et al. Safety and Efficacy: Clinical Experience of Venetoclax in Combination With Hypomethylating Agents in Both Newly Diagnosed and Relapsed/Refractory Advanced Myeloid Malignancies. Hemasphere. 2021 Mar 9;5(4):e549.		1
Gemici A, Ozkalemkas F, Dogu MH, et al. A Real-life Turkish Experience of Venetoclax Treatment in High-risk Myelodysplastic Syndrome and Acute Myeloid Leukemia. Clin Lymphoma Myeloma Leuk. 2021 Aug;21(8):e686-e692.		1
Ball BJ, Famulare CA, Stein EM, et al. Venetoclax andhypomethylating agents (HMAs) induce high responserates in MDS, including patients after HMA therapyfailure. Blood Adv. 2020;4(13):2866–2870.		2

Bewersdorf JP, Derkach A, Gowda L, et al. Venetoclax-based combinations in AML and high-risk MDS prior to and following allogeneic hematopoietic cell transplant. Leuk Lymphoma. 2021 Dec;62(14):3394-3401.		1
Azizi A, Ediriwickrema A, Dutta R, et al. Venetoclax and hypomethylating agent therapy in high risk myelodysplastic syndromes: a retrospective evaluation of a real-world experience. Leuk Lymphoma. 2020 Nov;61(11):2700-2707.		2
Winters AC, Maloney KW, Treece AL, Gore L, Franklin AK. Single-center pediatric experience with venetoclax and azacitidine as treatment for myelodysplastic syndrome and acute myeloid leukemia. Pediatr Blood Cancer. 2020 Oct;67(10):e28398.		1
Schuler E, Wagner-Drouet EM, Ajib Set al. Treatment of myeloid malignancies relapsing after allogeneic hematopoietic stem cell transplantation with venetoclax and hypomethylating agents-a retrospective multicenter analysis on behalf of the German Cooperative Transplant Study Group. Ann Hematol. 2021 Apr;100(4):959-968.		1

Ganan-Gomez I, Yang H, Ma F, et al. Stem cell architecture drives myelodysplastic syndrome progression and predicts response to venetoclax-based therapy. Nat Med. 2022 Mar;28(3):557-567.		4
Gangat N, McCullough K, Johnson I, et al. Real-world experience with venetoclax and hypomethylating agents in myelodysplastic syndromes with excess blasts. Am J Hematol. 2022 Jun 1;97(6):E214-E216.		4
Gao F, Gao Y, Luo Y, et al. Venetoclax plus hypomethylating agent for the salvage treatment of relapsing myeloid malignancies after hematopoietic stem cell transplantation: A multicenter retrospective study on behalf of the Zhejiang Cooperative Group for Blood and Marrow Transplantation. Am J Hematol. 2022 Feb 1;97(2):E44-E47.		4
Shimony S, Stone RM, Stahl M. Venetoclax combination therapy in acute myeloid leukemia and myelodysplastic syndromes. Curr Opin Hematol. 2022 Mar 1;29(2):63-73.		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
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Todd Gersten	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
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases		B
John Roberts	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	In 5 prospective trials and 11 retrorespective reports of venetoclax in combination with azacitidine or decitabine, response rates were relatively high (~65%), response durations were measured in months, many months, and toxicities were moderate. Follow-up times ranged from 5 to 23 months, and mortality was ~ 45%. Venetoclax doses ranged widely, and optimal doses are not known. Many agents are used to treat myelodysplastic syndrome, and at this time there is no meaningful comparative data.	

Richard LoCicero	Evidence Favors Efficacy	Class III: Not Recommended	A systemic review and meta-analysis has reported outcomes after MDS treatment with Venetoclax in combination with hypomethylating agents (azacitidine or decitabine). Eleven retrospective studies and five phase 1b clinical trials were included. While reported efficacy was favorable, prospective later phase trials will be necessary to establish the role for standard treatment.	
Todd Gersten	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	Venetoclax combined with a hypomethylating agent in patients myelodysplastic syndrome resulted in promising response rates and overall survival in pooled analyses in a systematic review/meta-analysis	