Clinical Criteria

Subject:	Vidaza (azacitidine)		
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Overview

This document addresses the use of Vidaza (azacitidine). Vidaza is a nucleoside metabolic inhibitor used for treatment of myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML) under specific conditions.

In 2004, Vidaza was FDA approved to treat French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL). Since the initial trials of Vidaza for MDS, new classification systems, such as World Health Organization (WHO) diagnostic criteria and the International Prognostic Scoring System and response criteria guidelines have been developed and revised. As a result, many of the patients in studies for MDS met criteria for having AML, validating the use of this agent in AML under certain conditions.

Vidaza is also indicated in combination with Tibsovo (ivosidenib) for the treatment of newly diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Vidaza. These include single agent use for induction and postremission therapy in individuals 60 years of age and older who need low-intensity treatment. NCCN also recommends Vidaza for relapsed or refractory disease in individuals who cannot tolerate more aggressive regimen, as a single agent or in combination with venetoclax. It is also recommended in combination with sorafenib for FLT3-ITD mutation positive disease. NCCN recommends Vidaza in combination with Venclexta (venetoclax) as induction or post-remission therapy for individuals 60 years of age and older who are not candidates for intensive remission induction therapy. Venclexta (venetoclax) has received accelerated approval for treatment of AML in combination with azacitidine in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

In addition, NCCN notes the following: “The 2016 WHO classification for AML includes entity ‘AML with myelodysplasia-related changes’ that encompasses patients who were previously categorized in the FAB classification of MDS as RAEB-T. AML evolving from MDS (AML-MDS) is often more resistant to cytotoxic chemotherapy than AML that arises without antecedent hematologic disorder and may have a more indolent course.” Similarly, myelofibrosis progressing to advanced phase/AML is treated according to the AML guidelines.

Definitions and Measures

Myelodysplastic syndrome (MDS): A condition that occurs when the blood-forming cells in the bone marrow are damaged.

- Primary MDS: Initial MDS diagnosis, usually when a cause is unknown.
- Secondary MDS: When a cause for the disease is known. Common causes include earlier treatment for a cancer; also known as treatment-related MDS.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Vidaza (azacitidine)

Requests for Vidaza (azacitidine) may be approved if the following criteria are met:

I. Individual has a diagnosis of myelodysplastic syndrome (MDS);

OR

II. Individual has a diagnosis of acute myelogenous leukemia (AML), and one of the following are met (NCCN 2A):
   A. Azacitidine is used as a single agent for individuals 60 years of age and older or individuals who cannot tolerate more aggressive regimens; **OR**
   B. Azacitidine is used in combination with venetoclax for individuals ~~75~~60 years of age and older or individuals who cannot tolerate more aggressive regimens (NCCN 2A, DiNardo 2019, DiNardo 2020); **OR**
   C. Azacitidine is used in combination with venetoclax for individuals with unfavorable risk genetics or TP53-mutated AML; **OR**
   ~~C.~~D. Azacitidine is used in combination with sorafenib for relapsed or refractory AML with FLT3-ITD mutations; **OR**
   ~~D.~~E. Azacitidine is used in combination with ivosidenib (Tibsovo) for newly diagnosed AML with a susceptible IDH1 (isocitrate dehydrogenase-1) mutation in adults ~~75~~60 years of age or older, or who have comorbidities that preclude use of intensive induction chemotherapy (which includes at least one of the following: baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2, severe cardiac or pulmonary disease, hepatic impairment with bilirubin > 1.5 times the upper limit of normal, creatinine clearance < 45 mL/min, or other comorbidity) (Tibsovo Label); **OR**
   ~~E.~~F. Individual has AML arising from MDS.

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Requests for Vidaza (azacitidine) may not be approved for the following:

I. Individual has advanced malignant hepatic tumors; **OR**
II. When the above criteria are not met or for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9025	Injection, azacitidine, 1 mg [Vidaza]

ICD-10 Diagnosis

C92.00-C92.02	Acute myeloblastic leukemia
C92.40-C92.42	Acute promyelocytic leukemia
C92.50-C92.52	Acute myelomonocytic leukemia
C92.60-C92.62	Acute myeloid leukemia with 11q23-abnormality
C92.A0-C92.A2	Acute myeloid leukemia with multilineage dysplasia
C93.00-C93.02	Acute monoblastic/monocytic leukemia
C93.10-C93.12	Chronic myelomonocytic leukemia
C94.00-C94.02	Acute erythroid leukemia
C94.40-C94.42	Acute panmyelosis with myelofibrosis
C94.6	Myelodysplastic disease, not classified
D46.0	Refractory anemia without ring sideroblasts, so stated

D46.1	Refractory anemia with ring sideroblasts (RARS)
D46.20-D46.22	Refractory anemia with excess of blasts (RAEB)
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts (RCMD RS)
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.4	Refractory anemia, unspecified
D46.Z	Other myelodysplastic syndromes
D46.9	Myelodysplastic syndrome, unspecified
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D75.81	Myelofibrosis

Document History

Revised: 08/19/2022
Document History:

- 08/19/2022 – Select Review: Update combination use with Tibsovo and Venclexta for AML to include minimum age of 60 per NCCN; allow combination use with Venclexta for those with unfavorable risk genetics per NCCN. Coding reviewed: No changes.
- 06/13/2022 – Select Review: Add FDA approval for combination use with Tibsovo for the treatment of newly diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. Add may not be approved criteria. Coding Reviewed: No Changes.
- 02/25/2022 – Annual Review: Add references to criteria. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: No changes. Coding reviewed: No changes.
- 02/21/2019 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/17/2019 – Annual Review: First review of Vidaza clinical criteria. Add references for off label criteria. Add use in combination with venetoclax for older patients with relapsed or refractory AML. Coding Reviewed: No changes.

References

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3. DiNardo CD, Pratz K, Pullarkat V, et al. Venetoclax combined with decitabine or azacitidine in treatment-naïve, elderly patients with acute myeloid leukemia. Blood 2019;133:7-17
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6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 20, 2022.
    a. Acute Myeloid Leukemia. V1.2022. Revised December 2, 2021.
    b. Myelodysplastic Syndromes. V3.2022. Revised January 13, 2022.
    c. Myeloproliferative Neoplasms. V2.2021. Revised August 18, 2021.