Clinical Policy: Azacitidine (Onureg, Vidaza)

Reference Number: LA.PHAR.387
Effective Date: 03.16.23
Last Review Date: 06.25.23 Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Azacitidine (Onureg®, Vidaza®) is a nucleoside metabolic inhibitor.

FDA Approved Indication(s)
Onureg is indicated for continued treatment of adult patients with acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

Vidaza is indicated for the treatment of:
- Adult patients with the following French-American-British (FAB) myelodysplastic syndrome (MDS) subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (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).
- Pediatric patients aged 1 month and older with newly diagnosed juvenile myelomonocytic leukemia (JMML).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Onureg and Vidaza are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. Myelodysplastic Syndromes (must meet all)**:**
1. Diagnosis of MDS, including JMML;
2. Request is for Vidaza;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. One of the following (a or b):
   a. Age ≥ 18 years;
   b. Age ≥ 1 month, and request is for JMML;
5. Request meets one of the following (a, b, or c):*
   a. For MDS, dose does not exceed one of the following (i or ii):
      i. Initial: 75 mg/m^2 per day for 7 days;
      ii. Maintenance: 100 mg/m^2 per day for 7 days per 4-week cycle;

b. For JMML, dose does not exceed one of the following administered daily for 7 days per 28-day cycle, for up to 6 cycles (i or ii):
   i. Age 1 month to less than 1 year or weighing less than 10 kg: 2.5 mg/kg;
   ii. Age 1 year and older and weighing 10 kg or greater: 75 mg/m^2;
c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Acute Myeloid Leukemia (Vidaza off-label) (must meet all)**:**

1. Diagnosis of AML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Onureg requests, member meets all of the following (a, b, c, and d):
   a. Request is for maintenance therapy;
   b. Request is for single-agent therapy;
   c. Member achieved CR or CRi following intensive induction chemotherapy and is either not able or declines to complete intensive consolidation/curative therapy (*see Appendix D*);
   d. One of the following (i or ii):
      i. Medical justification supports inability to use SC/IV azacitidine (e.g., contraindication to excipients);
      ii. For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
5. For Onureg requests, member must use generic azacitidine, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a, b, or c):*
   a. Onureg: Dose does not exceed 300 mg (1 tablet) per day for 14 days per 4-week cycle;
   b. Vidaza: Dose does not exceed 100 mg/m^2 per day for 7 days per 4-week cycle;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Myelofibrosis (off-label) (must meet all)**:**

1. Diagnosis of advanced phase (i.e., accelerated- or blast-phase) myelofibrosis (MF);
2. Request is for Vidaza;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg/m^2 per day for 7 days per 4-week cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Vidaza or Onureg for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Onureg requests, member must use generic azacitidine, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, c, or d):*
   a. Onureg: New dose does not exceed 300 mg (1 tablet) per day for 14 days per 4-week cycle;
   b. Vidaza for MDS: New dose does not exceed 100 mg/m^2 per day for 7 days per 4-week cycle;
   c. Vidaza for JMML: New dose does not exceed one of the following administered daily for 7 days per 28-day cycle, for up to 6 cycles (i or ii):
      i. Age 1 month to less than 1 year or weighing less than 10 kg: 2.5 mg/kg;
      ii. Age 1 year and older and weighing 10 kg or greater: 75 mg/m^2;
   d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

   Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myelogenous leukemia
ANC: absolute neutrophil count
CMMoL/CMML: chronic myelomonocytic leukemia
CR: complete response
CRi: complete response with incomplete hematologic recovery
FAB: French-American-British
FDA: Food and Drug Administration
JMML: juvenile myelomonocytic leukemia
MDS: myelodysplastic syndrome
MF: myelofibrosis
NCCN: National Comprehensive Cancer Network
RA: refractory anemia
RAEB: refractory anemia with excess blasts
RAEB-T: refractory anemia with excess blasts in transformation
RARS: refractory anemia with ringed sideroblasts

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings:
- Contraindication(s): advanced malignant hepatic tumors (Vidaza only), hypersensitivity to azacitidine (or mannitol for Vidaza only)
- Boxed warning(s): none reported

Appendix D: General Information
The National Comprehensive Cancer Network (NCCN) AML treatment guidelines define morphologic CR in patients that are independent of transfusions as follows:
- Absolute neutrophil count (ANC) > 1,000/mcL (blasts < 5%)
- Platelets ≥ 100,000/mcL (blasts < 5%)

NCCN presents CRi (a variant of CR) for AML as follows based on clinical trial information:
- < 5% marrow blasts
- Either ANC < 1,000/mcL or platelets < 100,000/mcL
- Transfusion independence but with persistence of neutropenia (<1,000/mcL) or thrombocytopenia (<100,000/mcL)

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Azacitidine (Onureg)	AML	300 mg PO QD on days 1 through 14 of each 28-day cycle	300 mg/day for 14 days/cycle
Azacitidine (Vidaza)	MDS	75 mg/m^2 SC or IV infusion QD for 7 days. Repeat cycle every 4 weeks. May increase to 100 mg/m^2 (after 2 treatment cycles). Patients should be treated for a minimum of 4 to 6 cycles. Doses may be adjusted or delayed based on hematology lab values, renal function, or serum electrolytes.	100 mg/m^2/day for 7 days/cycle

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Continue treatment as long as the patient continues to benefit	
	JMML	Age 1 month to less than 1 year or weighing less than 10 kg: 2.5 mg/kg Age 1 year and older and weighing 10 kg or greater: 75 mg/m^2 Administer IV daily for 7 days in a 28-day cycle, for a minimum of 3 cycles and a maximum of 6 cycles	See dosing regimen

VI. Product Availability

Drug Name	Availability
Azacitidine (Onureg)	Tablets: 200 mg, 300 mg
Azacitidine (Vidaza)	Lyophilized powder in single dose vials: 100 mg

VII. References

1. Onureg Prescribing Information. Summit, NJ: Celgene Corporation; May 2021. Available at: https://onuregpro.com. Accessed August 1, 2022.
2. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; May 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/050974s034lbl.pdf. Accessed August 1, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 1, 2022.
4. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2022. Available at http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 1, 2022.
5. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 2.2022. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 1, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9025	Injection, azacitidine, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy	02.23	03.16.23

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Updated criteria for other diagnoses/indications Added Onureg to the policy and Onureg specific criteria	06.25.23	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.