

Clinical Policy: Azacitidine (Onureg, Vidaza)

Reference Number: LA.PHAR.387

Effective Date: 03.16.23

Last Review Date: 06.25.23

Line of Business: Medicaid

Coding Implications

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 (CMML).
- Pediatric patients aged 1 month and older with newly diagnosed juvenile myelomonocytic leukemia (JMML).

Policy/Criteria

~~Prior authorization is required.~~ 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 ~~is~~**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 \geq 18 years;
 - b. Age \geq 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/m² per day for 7 days;
 - ii. Maintenance: 100 mg/m² 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/m²;
- 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.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;
- 4.6. 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;
 - a.b. Vidaza: Dose does not exceed 100 mg/m² per day for 7 days per 4-week cycle;
 - b.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

D.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/m² 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

E.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
- ~~1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.~~

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;
- ~~3-4.~~ If request is for a dose increase, request meets one of the following (a-~~or~~, b, c, or d):*
 - a. Onureg: New dose does not exceed 300 mg (1 tablet) per day for 14 days per 4-week cycle;
 - a.b. Vidaza for MDS: New dose does not exceed 100 mg/m² per day for 7 days per 4-week cycle;
 - b.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/m²;
 - e.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):

- ~~b. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.~~
- ~~Approval duration: Duration of request or 6 months (whichever is less); or~~
- ~~3. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.~~
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 \geq 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
<u>Azacitidine (Onureg)</u>	<u>AML</u>	<u>300 mg PO QD on days 1 through 14 of each 28-day cycle</u>	<u>300 mg/day for 14 days/cycle</u>
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. Continue treatment as long as the patient continues to benefit	100 mg/m ² /day for 7 days/cycle
	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
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.

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recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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