

## Clinical Policy: Azacitidine (Onureg, Vidaza)

Reference Number: PA.CP.PHAR.387

Effective Date: 10/2018

Last Review Date: 10/2023

[Coding Implications](#)  
[Revision Log](#)

### Description

Azacitidine (Onureg<sup>®</sup>, Vidaza<sup>®</sup>) 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

*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 PA Health & Wellness<sup>®</sup> that Onureg<sup>®</sup> 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  $\geq$  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/m<sup>2</sup> per day for 7 days;
    - ii. Maintenance: 100 mg/m<sup>2</sup> 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<sup>2</sup>;
- c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**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  $\geq$  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. Request is for is for Stage IV or metastatic cancer;
- 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<sup>2</sup> 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*).

**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  $\geq$  18 years;
- 5. Request meets one of the following (a or b):
  - a. Dose does not exceed 100 mg/m<sup>2</sup> 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*).

**Approval duration:** 6 months

**D. Other diagnoses/indications**

- 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): PA.CP.PMN.53.

## II. Continued Therapy

### A. All Indications in Section I (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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<sup>2</sup> 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<sup>2</sup>;
  - d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration:** 12 months

### B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.  
**Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.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 – PA.CP.PMN.53 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
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 <sup>2</sup> SC or IV infusion QD for 7 days. Repeat cycle every 4 weeks. May increase to 100 mg/m <sup>2</sup> (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 <sup>2</sup> /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 <sup>2</sup>  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**

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

**VIII. References**

1. Onureg Prescribing Information. Summit, NJ: Celgene Corporation; October 2022. Available at: <https://onuregpro.com>. Accessed June 30, 2023.
2. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; May 2022. Available at: <https://www.vidaza.com>. Accessed June 30, 2023.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed June 30, 2023.
4. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 1.2023. Available at [http://www.nccn.org/professionals/physician\\_gls/pdf/mds.pdf](http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf). Accessed June 30, 2023.
5. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 4.2023. Available at [http://www.nccn.org/professionals/physician\\_gls/pdf/aml.pdf](http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf). Accessed June 30, 2023.

**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	P&T Approval Date
Policy created	10/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
4Q 2020 annual review: MDS, MF, AML criteria collapsed in recognition of the interrelated transformative nature of the three disease states and to encompass new subtypes and treatment algorithms; references reviewed and updated.	10/2020	
4Q 2021 annual review: RT2: added Onureg to policy; added criteria that Onureg be administered as single-agent therapy and option that member could decline consolidation/curative therapy for Onureg request per NCCN compendium; updated NCCN definition of CR and CRi in General Information and Appendix D; for Onureg requests, added requirement for use of generic if available; references reviewed and updated.	10/2021	

<b>Reviews, Revisions, and Approvals</b>	<b>Date</b>	<b>P&amp;T Approval Date</b>
4Q 2022 annual review: added additional indication for Vidaza in pediatric patients aged 1 month and older with newly diagnosed JMML per updated prescribing information; generalized oncology redirection bypass language; references reviewed and updated.	10/2022	
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023	