Clinical Policy: Azacitidine (Onureg, Vidaza)

Reference Number: PA.CP.PHAR.387
Effective Date: 10/2018
Last Review Date: 10/2025

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 PA Health & Wellness® that azacitidine, 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 generic azacitidine or 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. For brand Vidaza requests, member must use generic azacitidine, unless contraindicated or clinically significant adverse effects are experienced;
6. 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*).

Approval duration: 12 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, all of the following (a, b, c, and d):
   a. Request is for maintenance therapy;
   b. Prescribed as a single agent;
   c. Member achieved CR or CRi following intensive induction (*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 Vidaza requests, prescribed in one of the following ways (a-f):
   a. As a single agent;
   b. In combination with Venclexta®;
   c. For relapsed or refractory disease with FLT3-ITD (internal tandem duplication) mutation: In combination with Nexavar®;
   d. For IDH1 mutation: In combination with Tibsovo®;
   e. For IDH2 mutation: In combination with Idhifa®;
   f. For FLT3-ITD or TKD (tyrosine kinase domain) mutation in disease without IDH1 mutation: In combination with Xospata®;
6. For brand product requests, member must use generic azacitidine, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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*).

Approval duration: 12 months

C. Myeloproliferative Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of advanced phase (i.e., accelerated- or blast-phase) myeloproliferative neoplasms;
2. Request is for generic azacitidine or Vidaza;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;

5. Prescribed as bridging therapy prior to transplant, unless member is not a candidate for transplant;
6. One of the following (a or b):
   a. Prescribed as a single agent or in combination with Jakafi®, Inrebic®, Ojjaara®, or Vonjo® for palliation of splenomegaly or other disease-related symptoms;
   b. Prescribed in combination with Venclexta;
7. For brand Vidaza requests, member must use generic azacitidine, unless contraindicated or clinically significant adverse effects are experienced;
8. 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*).

Approval duration: 12 months

D. Peripheral T-Cell Lymphoma (off-label) (must meet all)**:**

1. Diagnosis of one of the following peripheral T-cell lymphomas (a, b, or c):
   a. Angioimmunoblastic T-cell lymphoma;
   b. Nodal peripheral T-cell lymphoma with TFH phenotype;
   c. Follicular T-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed, refractory or progressive;
5. Prescribed as a single agent for one of the following (a or b):
   a. Initial palliative therapy;
   b. Second-line or subsequent therapy;
8. For Onureg requests, one of the following (a or b):
   a. Medical justification supports inability to use SC/IV azacitidine (e.g., contraindication to excipients);
   b. Request is for is for Stage IV or metastatic cancer;
6. For brand product requests, member must use generic azacitidine, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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*).

Approval duration: 12 months

E. 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.PHARM.01) applies;
2. Member is responding positively to therapy;
3. For brand product 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*).

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.PHARM.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
ITD: internal tandem duplication
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

TKD: tyrosine kinase domain

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. 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

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 July 11, 2025.
2. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; January 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/050794s036lbl.pdf. Accessed July 11, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 15, 2025.
4. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 2.2025. Available at http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed July 15, 2025.
5. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 2.2025. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 15, 2025.

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
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
4Q 2022 annual review: added additional indication for Vidaza in pediatric patients aged 1 month and older with newly diagnosed JMML per updated	10/2022

Reviews, Revisions, and Approvals	Date
prescribing information; generalized oncology redirection bypass language; references reviewed and updated.	
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: revised policy/criteria section to also include generic azacitidine; for all indications where applicable, updated generic redirection to include Vidaza; for AML, removed requirement for Onureg that member is not able to or declines to complete intensive consolidation therapy and added requirements regarding usage of Vidaza (single agent and combination) per NCCN; updated off-label criteria for "myelofibrosis" to instead refer to "myeloproliferative neoplasms" and added specific requirements around recommended uses (bridging therapy prior to transplant and use as a single agent or in various combinations) per NCCN; added off-label criteria for peripheral T-cell lymphomas per NCCN; references reviewed and updated.	10/2024
4Q 2025 annual review: for AML, added that use with Nexavar must be for relapsed or refractory disease per NCCN; extended initial approval durations from 6 to 12 months; references reviewed and updated.	10/2025