Clinical Policy: Azacitidine (Onureg, Vidaza)

Reference Number: ERX.SPA.275
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Azacitidine (Onureg®, Vidaza®) is a pyrimidine nucleoside analog of cytidine.

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 patients with the following French-American-British (FAB) myelodysplastic syndrome (MDS) subtypes: refractory anemia (RA), 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).

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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;
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, b, or c):*:
   a. Initial: Dose does not exceed 75 mg/m^2 per day for 7 days;
   b. Maintenance: 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

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. Medical justification supports inability to use SC/IV azacitidine (e.g., contraindication to excipients);

5. 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:
Medicaid – 6 months
Commercial - Onureg: Length of Benefit; Vidaza: 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
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Vidaza for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Onureg: New dose does not exceed 300 mg (1 tablet) per day for 14 days per 4-week cycle;
   b. Vidaza: New dose does not exceed 100 mg/m^2 per day for 7 days per 4-week cycle;
   c. 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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
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. Continue treatment as long as the patient continues to benefit	100 mg/m^2/day for 7 days/ cycle

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://packageinserts.bms.com/pi/pi_onureg.pdf. Accessed August 6, 2021.

2. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; March 2020. Available at: https://packageinserts.bms.com/pi/pi_vidaza.pdf. Accessed August 6, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 6, 2021.
4. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2021. Available at http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 6, 2021.
5. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2021. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 6, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
4Q 2019 annual review: MDS – modified trial requirement from an ESA to an ESA AND Revlimid for patients without 5q and EPO ≤ 500 and added options for use as bridge therapy while awaiting HSCT donor availability or in patients with clinically relevant thrombocytopenia/neutropenia or increased bone marrow blasts per NCCN; AML for members ≥ 60 years – added combination use with Nexavar and Venclexta and simplified uses as Vidaza can be used for both induction and maintenance therapy in elderly patients declining more aggressive therapy per NCCN; references reviewed and updated.	08.27.19	11.19
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; RT2: added Onureg to policy; references reviewed and updated.	09.09.20	11.20
4Q 2021 annual review: 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; Onureg approval duration changed to length of benefit for commercial line of business; updated NCCN definition of CR and CRi in General Information and Appendix D; references reviewed and updated.	08.01.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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