

Clinical Policy: Azacitidine (Vidaza)

Reference Number: CP.PHAR.387

Effective Date: 08.28.18

Last Review Date: 11.19

Line of Business: Commercial, HIM, Medicaid

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

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Azacitidine (Vidaza[®]) is a pyrimidine nucleoside analog of cytidine.

FDA Approved Indication(s)

Vidaza is indicated for the treatment of 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).

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 health plans affiliated with Centene Corporation[®] that Vidaza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Myelodysplastic Syndromes (must meet all):**

1. Diagnosis of MDS;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. Member meets one of the following (a, b, c, d, or e):
 - a. With del(5q) cytogenetic abnormality: Failure of Revlimid[®] at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Revlimid*
 - b. Without del(5q) cytogenetic abnormality and serum erythropoietin \leq 500 mU/mL: Failure of Revlimid and one of the following agents, unless all are contraindicated or clinically significant adverse effects are experienced: epoetin alfa (e.g., Epogen[®], Procrit[®], Retacrit[™]), Aranesp[®];
**Prior authorization may be required for Revlimid, epoetin alfa, and Aranesp*
 - c. Without del(5q) cytogenetic abnormality and serum erythropoietin $>$ 500 mU/mL;
 - d. Has previously received stem cell transplantation, will be receiving azacitidine as a bridge while awaiting stem cell transplant donor availability, or is not a candidate for stem cell transplant;

- e. Clinically relevant (e.g., clinically severe) thrombocytopenia or neutropenia, or increased bone marrow blasts (*see Appendix D*);
5. Request meets one of the following (a, b, or c):*
 - a. Initial: Dose does not exceed 75 mg/m² per day for 7 days;
 - b. Maintenance: Dose does not exceed 100 mg/m² 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/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

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

1. Diagnosis of acute myeloid leukemia (AML);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed for one of the following (a, b, or c):
 - a. In members age ≥ 60 years for one of the following (i, ii, or iii):
 - i. As a single agent;
 - ii. In combination with Nexavar[®] for FLT3-ITD mutation-positive disease;
**Prior authorization may be required for Nexavar*
 - iii. In combination with Venclexta[®];
**Prior authorization may be required for Venclexta*
 - b. Relapsed/refractory disease for one of the following (i, ii, or iii):
 - i. As a component of repeating the initial successful induction regimen if late relapse (≥ 12 months);
 - ii. As a single agent;
 - iii. In combination with Nexavar for FLT3-ITD mutation-positive disease;
**Prior authorization may be required for Nexavar*
 - c. Treatment of myelofibrosis (MF)-accelerated phase or MF-blast phase/acute myeloid leukemia;
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:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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 or b):*
 - a. New dose does not exceed 100 mg/m² per day for 7 days per 4-week cycle;
 - b. 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:

Medicaid/HIM – 12 months

Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myelogenous leukemia

CMMoL: chronic myelomonocytic leukemia

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

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
Procrit [®] , Epogen [®] , Retacrit [®] (epoetin alfa)*	150 to 300 units/kg/day SC or 450 to 1,000 units/kg/day SC in divided doses 3 to 7 times per week or 60,000 units every week	Target hemoglobin up to 12 g/dL
Aranesp [®] (darbepoetin alfa)*	150 to 300 mcg SC every week or 500 mcg SC every 2 to 3 weeks	Target hemoglobin up to 12 g/dL
Revlimid [®] (lenalidomide)	10 mg PO QD; dosing is modified based upon clinical and laboratory findings	25 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

**Off-label*

Appendix C: Contraindications/Boxed Warnings:

- Contraindication(s): advanced malignant hepatic tumors, hypersensitivity to azacitidine or mannitol
- Boxed warning(s): none reported

Appendix D: General Information

- The National Comprehensive Cancer Network (NCCN) guideline for MDS recommends the use of Vidaza or Dacogen for initial active therapy for all subtypes of MDS with the exception of patients with 5q cytogenetic abnormality or patients with serum erythropoetin levels not more than 500 mU/mL; these patients should be treated with Revlimid and/or an erythropoietic agent such as Procrit.
- Vidaza use for AML in elderly patients (≥ 60 years old) who are not considered eligible to receive conventional induction therapy or decline intensive therapy has an American Hospital Formulary Service (AHFS) Grade of Recommendation of reasonable (accepted), an NCCN Category rating of 2A, and is listed as an off-label indication in Clinical Pharmacology.
- Vidaza use for relapsed or refractory AML in patients who cannot tolerate more aggressive regimens has an NCCN Category rating of 2A and is listed as an off-label indication in Clinical Pharmacology.
- RAEB-T has been reclassified as AML with multilineage dysplasia in World Health Organization (WHO) system.
- Per the revised International Prognostic Scoring System (IPSS) for MDS, clinically significant cytopenias and blast count in the setting of MDS (i.e., those which worsen the prognostic score of MDS) are:
 - Platelets $< 100,000$;
 - Absolute neutrophil count < 800 ;
 - Blast count $> 2\%$.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MDS	75 mg/m ² SC or IV infusion QD for 7 days. Repeat cycle every 4 weeks. May increase to 100	100 mg/m ² /day for 7 days/cycle

Indication	Dosing Regimen	Maximum Dose
	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	

VI. Product Availability

Lyophilized powder in single dose vials: 100 mg

VII. References

1. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; September 2018. Available at: <http://media.celgene.com/content/uploads/vidaza-pi.pdf>. Accessed July 30, 2019.
2. Micromedex[®] Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 14, 2018.
3. Clinical Pharmacology [database online] Tampa, FL: Gold Standard, Inc.; 2019. Available at <http://www.clinicalpharmacology-ip.com>.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 30, 2019.
5. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 2.2019. Available at http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 12, 2019.
6. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2019. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 12, 2019.
7. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 2.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed August 12, 2019.
8. Greenberg PL, Tuechler H, Schanz J, et al. Revised International Prognostic Scoring System (IPSS-R) for myelodysplastic syndrome. Blood. 2012; 120: 2454-2465.

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
Converted to new template. Minor changes to verbiage and grammar. References updated. Updated NCCN Compendium supported uses for AML.	06.15.17	11.17
Policy created: adapted from previously approved policy CP.CPA.295 (retired); specialist requirement added; age requirement added; for MDS, added option for member to have serum EPO > 500 mU/mL without 5q cytogenetic abnormality or received/not a candidate for stem cell transplant; initial max dosing added; updated NCCN-compendium supported uses for AML; modified approval duration from length of benefit to 6 months or to member’s renewal date for commercial; references reviewed and updated.	08.28.18	11.18
4Q 2019 annual review: MDS – 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

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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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