Clinical Policy: Azacitidine (Vidaza)

Reference Number: PA.CP.PHAR.387
Effective Date: 10.17.18
Last Review Date: 10.17.18

Coding Implications
Revision Log

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 (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.

It is the policy of health plans affiliated with PA Health & Wellness® 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. Member meets one of the following (a, b, c, or d):
   a. With 5q cytogenetic abnormality: Failure of a trial 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 5q cytogenetic abnormality and serum erythropoietin ≤ 500 mU/mL: Failure of a trial 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®), Aranesp®;
      **Prior authorization may be required for Revlimid, epoetin alfa, and Aranesp*
   c. Without 5q cytogenetic abnormality and serum erythropoietin > 500 mU/mL;
   d. Has previously received stem cell transplantation or is not a candidate for stem cell transplant;
4. Dose does not exceed:
   a. Initial: 75 mg/m^2 per day for 7 days;
   b. Maintenance: 100 mg/m^2 per day for 7 days per cycle.

Approval duration: 6 months

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

1. Diagnosis of AML;

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Prescribed for one of the following (a, b, or c):
   a. As a single agent in members age ≥ 60 years for one of the following (i, ii, or iii):
      i. Lower-intensity induction therapy in candidates for intensive remission induction therapy with unfavorable cytogenetic or molecular markers/ antecedent hematologic disorder/ therapy-related AML;
      ii. Lower-intensity therapy in non-candidates for intensive remission induction therapy or those who decline intensive therapy;
      iii. Post-remission maintenance therapy following complete response to prior intensive therapy;
      iv. Post-remission therapy following response to prior lower intensity therapy;
   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 in patients who cannot tolerate more aggressive regimens;
      iii. As combination use 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;
   d. In combination with venetoclax in members age ≥ 60 years for one of the following (i, ii, or iii):
      i. Treatment induction in candidates for intensive remission induction therapy with unfavorable cytogenetic/molecular markers/antecedent hematologic disorder/therapy-related AML;
      ii. Treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy;
      iii. Post-remission therapy following response to previous lower intensity therapy with the same regimen;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 100 mg/m^2 per day for 7 days/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

C. 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 Pennsylvania Health and 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. If request is for a dose increase, new dose meets one of the following (a or b):
   a. Dose does not exceed 100 mg/m^2 per day for 7 days/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

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

1. Currently receiving medication via Pennsylvania Health and 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
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 1000 units/kg/day SC in divided doses 3 to 7 times per week or 60,000 units qweekly	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 or an erythropoietic agent such as Procrit, respectively.
- Vidaza use for untreated AML in elderly patients (>60 years old) who are not considered eligible to receive conventional induction therapy has an American Hospital Formulary Service (AHFS) Grade of Recommendation of reasonable (accepted), an NCCN Category rating of 2A for induction therapy, and is listed as an off-label indication in Clinical Pharmacology.
- Vidaza use for relapse 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.

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 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.	100 mg/m^2/day for 7 days/cycle

VI. Product Availability

Lyophilized powder in single dose vials: 100 mg

VII. References

1. Vidaza Prescribing Information. Summit, NJ: Celgene Corporation; July 2018. Available at: http://media.celgene.com/content/uploads/vidaza-pi.pdf. Accessed August 14, 2018.
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.; 2018. 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 June 19, 2017.

5. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 1.2019. Available at http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 14, 2018.
6. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 1.2018. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 14, 2018.
7. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 2.2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed August 14, 2018.

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	10/18	