RXADVANCE
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Clinical Policy Title: **Azacitidine (Vidaza)**
Policy Number: **RxA.549**
Drug(s) Applied: **Azacitidine (Vidaza®)**
Last Review Date: **01/2020**
Line of Business: **Commercial, HIM, Medicaid**

Background

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

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

Lyophilized powder in single dose vials: 100 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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 ≥ 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 ≤ 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/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:
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/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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

II. Continued Therapy

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

1. Currently receiving medication via RxAdvance 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/m^2 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

III. Appendices

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:
  o Platelets < 100,000;
  o Absolute neutrophil count < 800;
  o Blast count > 2%.

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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	03/06/2020