Clinical Policy: Azacitidine (Vidaza)
Reference Number: ERX.SPA.275
Effective Date: 08.28.18
Last Review Date: 11.18

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), 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 Envolve Pharmacy Solutions™ 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 ≥ 18 years;
   4. 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 one of the following agents, unless all are contraindicated or clinically significant adverse effects are experienced: Procrit®, Aranesp®;
         *Prior authorization may be required for Procrit 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;
   5. Dose does not exceed:
      a. Initial: 75 mg/m² per day for 7 days;
      b. Maintenance: 100 mg/m² per day for 7 days per 4-week 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. Age ≥ 18 years;
   4. 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;

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).

Approval duration: 6 months

C. 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 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).

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
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 and may require prior authorization.*

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procrit® (epoetin alfa)*</td>
<td>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 weekly</td>
<td>Target hemoglobin up to 12 g/dL</td>
</tr>
<tr>
<td>Aranesp® (darbepoetin alfa)*</td>
<td>150 to 300 mcg SC every week or 500 mcg SC every 2 to 3 weeks</td>
<td>Target hemoglobin up to 12 g/dL</td>
</tr>
<tr>
<td>Revlimid® (lenalidomide)</td>
<td>10 mg PO QD; dosing is modified based upon clinical and laboratory findings</td>
<td>25 mg/day</td>
</tr>
</tbody>
</table>

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.

**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**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>75 mg/m² SC or IV infusion QD for 7 days. Repeat cycle every 4 weeks. May increase to 100 mg/m² (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.</td>
<td>100 mg/m²/day for 7 days/cycle</td>
</tr>
</tbody>
</table>

**VI. Product Availability**

Lyophilized powder in single dose vials: 100 mg
VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
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<td>Policy created</td>
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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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