I. Medication Description

Azacitidine is a pyrimidine nucleoside analog of cytidine. Azacitidine is believed to exert its antineoplastic effects by causing hypomethylation of DNA and direct cytotoxicity on abnormal hematopoietic cells in the bone marrow. Hypomethylation may restore normal function to genes that are critical for differentiation and proliferation. The cytotoxic effects of azacitidine cause the death of rapidly dividing cells, including cancer cells that are no longer responsive to normal growth control mechanisms. Non-proliferating cells are relatively insensitive to azacitidine.

II. Position Statement

- Requests for use with certain diagnostic codes do not require prior authorization and supporting clinical documentation. See Addendum.
- Coverage is determined through a prior authorization process with supporting clinical documentation for all other requests.

III. Policy

Coverage of Vidaza is provided when prescribed by an oncologist AND when used for one of the following indications:

- **Acute Myeloid Leukemia:**
  - When used as a single agent in patients at least 60 years of age as either induction therapy, postremission therapy, or maintenance therapy following complete response to prior cytarabine therapy OR
  - When used for relapsed or refractory disease in patients who cannot tolerate more aggressive regimens as a single agent or in combination with sorafenib (FLT3-ITD positive).

- **Myelodysplastic Syndromes:**
  - Initial treatment in lower-risk patients with
    - symptomatic anemia and serum erythropoietin levels >500 mU/ml with no del(5q) and a low probability of response to immunosuppressive therapy OR
    - clinically relevant thrombocytopenia or neutropenia, or increased marrow blasts
  - Treatment in lower-risk patients with symptomatic anemia, del(5q), and serum erythropoietin levels >500 mU/ml with either no response or intolerance to lenalidomide therapy and a low probability of response to immunosuppressive therapy
  - Treatment in lower-risk patients with symptomatic anemia and serum erythropoietin levels less than or equal to 500 mU/ml with no response to erythropoietins and no response or intolerance to immunosuppressive therapy
  - Treatment in higher-risk patients who are either nontransplant candidates or transplant candidates awaiting donor availability
  - Treatment in higher-risk patients who have no response from or relapse after allogeneic hematopoietic stem cell transplant.
• Myeloproliferative Neoplasms – Primary Myelofibrosis and Post-polycythemia vera (post-PV), or Post-essential thrombocytopenia (post-EF) myelofibrosis (MF)
  ○ Treatment of myelofibrosis (MF) – accelerated phase or MF-blast phase/acute myeloid leukemia

IV. Quantity Limitations

• Up to 98 vials every 6 months are covered (to allow for up to 14 vials every 4 weeks).
• Additional quantities may be considered if BSA exceeds 2m²

V. Coverage Duration

Coverage is granted for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:
• Stabilization of disease or in absence of disease progression AND
• Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

• Available as: 100mg single-dose vial
• J9025; 1 billable unit = 1mg azacitidine
• Pertinent indications:
  ○ AML: C92.00, C92.01, C92.02, C92.50, C92.51, C92.52, C92.60, C92.61, C92.62, C92.A0, C92.A1, C92.A2, C93.00-C93.02, C94.00-C94.02, C94.20-C94.22
  ○ MDS: C92.10, C92.12, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.Z, D46.9, D46.4
  ○ Myeloproliferative Neoplasms: C94.40-C94.42, C94.6, D47.1, D47.4, D75.81

VIII. Summary of Policy Changes

• 3/1/11: no changes
• 6/15/12: no changes
• 3/15/13: addition of autopay code for AML for Vidaza only
• 3/15/14: moved to own policy, quantity limits expanded, ICD10 codes added to policy for use starting 10/1/14.
• 3/15/15: addition of AML diagnosis codes for which coverage may be reviewed; updated MDS coverage to coincide with current NCCN guidelines
• 7/1/15: formulary distinctions made
• 10/1/15: omission of ICD9 references
• 3/15/16: policy updated to correspond with current NCCN treatment guidelines
• 1/1/17: policy updated to correspond with current NCCN treatment guidelines
IX. References


Addendum:

<table>
<thead>
<tr>
<th>ICD10</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9210</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission</td>
</tr>
<tr>
<td>C9211</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, in remission</td>
</tr>
<tr>
<td>C9212</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, in relapse</td>
</tr>
<tr>
<td>D460</td>
<td>Refractory anemia without ring sideroblasts, so stated</td>
</tr>
<tr>
<td>D461</td>
<td>Refractory anemia with ring sideroblasts</td>
</tr>
<tr>
<td>D4620</td>
<td>Refractory anemia with excess of blasts, unspecified</td>
</tr>
<tr>
<td>D4621</td>
<td>Refractory anemia with excess of blasts 1</td>
</tr>
<tr>
<td>D4622</td>
<td>Refractory anemia with excess of blasts 2</td>
</tr>
<tr>
<td>D46A</td>
<td>Refractory cytopenia with multilineage dysplasia</td>
</tr>
<tr>
<td>D46B</td>
<td>Refractory cytopenia with multilineage dysplasia and ring sideroblasts</td>
</tr>
</tbody>
</table>

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.