Pharmacy Policy Bulletin: J-1002 Oral Hypomethylating Agents - Commercial and Healthcare Reform	
Number: J-1002	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1002-008	**Original Date:** 10/07/2020
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Inqovi (decitabine/cedazuridine) • Onureg (azacitidine)

FDA-Approved Indication(s):	• Inqovi
	  ○ Treatment of adults with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System (IPSS) groups.
	• Onureg
	  ○ Treatment of adults with acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

Background:	• Inqovi is comprised of decitabine and cedazuridine. Decitabine acts as a hypomethylating agent, which may result in restoration of normal function to genes in cancer cells. Cedazuridine inhibits cytidine deaminase, an enzyme that degrades decitabine, to increase oral bioavailability of decitabine. • Onureg inhibits nucleosides to hypomethylate DNA, resulting in decreased cancerous cellular proliferation. • MDS are a rare group of blood disorders characterized by abnormally low blood cell counts due to abnormal development of blood cells by the bone marrow. MDS may progress to bone marrow failure or AML. Symptoms include anemia, bleeding, infection risk, and a risk of disease transformation to AML. • CMML is a clonal hematopoietic stem cell disorder that is characterized by the presence of sustained peripheral blood monocytosis with overlapping features of myelodysplastic syndromes and myeloproliferative neoplasms. CMML is classified as a disease state distinct from MDS.

	• Other hypomethylating agents approved for MDS include Dacogen (decitabine), administered intravenously (IV); and Vidaza (azacitidine), administered IV or subcutaneously (SC).
	• IPSS is a scoring system utilized to stratify MDS prognosis into four risk groups: low, intermediate-1, intermediate 2, and high risk. IPSS takes into account analysis of peripheral cytopenias, percentage of bone marrow blasts, and cytogenetic characteristics.
	• National Comprehensive Cancer Network (NCCN) guidelines for MDS stratify treatment recommendations per disease subtype.
	  ○ For IPSS Intermediate-2, high risk patients who are not transplant eligible, azacitidine is a preferred, category 1 recommendation (± venetoclax); decitabine ± venetoclax, oral decitabine and cedazuridine ± venetoclax, or clinical trial are category 2A recommendations.
	  ○ For IPSS intermediate-1 patients with clinically relevant thrombocytopenia or neutropenia or increased marrow blasts, azacitidine, decitabine, oral decitabine and cedazuridine, immunosuppressive (IST) therapy, or clinical trial are category 2A recommendations.
	• AML comprises a group of hematologic malignancies characterized by the proliferation of myeloid blast cells in the peripheral blood, bone marrow, and/or other tissues. AML is the most common form of acute leukemia among adults.
	• Curative therapy for AML may include stem cell transplant.
	• Prescribing Considerations:
	  ○ Hypomethylating agents should be prescribed by a hematologist/oncologist.
	  ○ Inqovi
	  ▪ Inqovi carries warnings and precautions for myelosuppression and embryo-fetal toxicity.
	  ▪ Monitoring parameters include obtaining a complete blood cell count prior to initiation of Inqovi, prior to each cycle, and as clinically indicated to monitor response and toxicity. Monitor patients with moderate renal impairment.
	  ▪ Inqovi should not be substituted for an IV decitabine product within a cycle.
	  ○ Onureg
	  ▪ Onureg has warnings or precautions for risks of substitution with other azacitidine products, myelosuppression, increased early mortality in patients with myelodysplastic syndromes, and embryo-fetal toxicity.
	  ▪ Onureg is contraindicated for use in patients with history of severe hypersensitivity to azacitidine or its components.
	  ▪ Complete blood counts should be monitored every other week for the first two cycles and prior to the start of each cycle thereafter. There are additional specifications for blood count monitoring after a dose reduction.
	  ▪ Onureg is not interchangeable with IV azacitidine.

Approval Criteria

I. Initial Authorization

A. Inqovi

When a benefit, coverage of Inqovi may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of one (1) of the following **(a. or b.)**:

a. Myelodysplastic syndromes (MDS, ICD-10: D46) when one (1) of the following criteria is met **(i. or ii.)**:

i. The member has been diagnosed with one (1) of the following French American-British MDS subtypes **(A), B), or C))**:
- **A)** Refractory anemia (ICD-10: D46.0)
- **B)** Refractory anemia with ringed sideroblasts (ICD-10: D46.1)
- **C)** Refractory anemia with excess blasts (ICD-10: D46.4)

ii. The member has a diagnosis of one (1) of the following International Prognostic Scoring System groups **(A), B), or C))**:
- **A)** Intermediate-1
- **B)** Intermediate-2
- **C)** High-risk

b. Chronic myelomonocytic leukemia (CMML, ICD-10: C93.1)

B. Onureg

When a benefit, coverage of Onureg may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of AML (ICD-10: C92).
3. The member achieved first CR or CRi following intensive induction chemotherapy.
4. The prescriber attests that the member is unable to complete intensive curative therapy.

II. Reauthorization

When a benefit, reauthorization of an oral hypomethylating agent may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:
1. Disease improvement
2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Inqovi [package insert]. Japan: Otsuka Pharmaceutical Co.; March 2022.

2. Onureg [package insert]. Summit, New Jersey: Celgene Corporation; May 2021.
3. National Organization for Rare Diseases. Myelodysplastic Syndromes. Available at: https://rarediseases.org/rare-diseases/myelodysplastic-syndromes/. Accessed July 2, 2025.
4. Dacogen [package insert]. Rockville, Maryland: Otsuka America Pharmaceutical, Inc.; June 2020.
5. Vidaza [package insert]. Summit, New Jersey: Celgene Corporation; June 2024.
6. NCCN Guidelines Version 2.2025. Myelodysplastic Syndromes. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed July 2, 2025.