Onureg® (azacitidine)
(Oral)

Document Number: IC-0565

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Dates Reviewed: 10/2020, 08/2021

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Onureg 200 mg tablets: 14 tablets per 28 days
- Onureg 300 mg tablets: 14 tablets per 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 300 mg on days 1 through 14 of a 28-day cycle

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Therapy will not be substituted for intravenous or subcutaneous azacitidine; **AND**
- Patient does not have a diagnosis of Myelodysplastic Syndrome (MDS); **AND**
- Patient does not have a hypersensitivity to another product containing azacitidine (i.e., Vidaza, etc.); **AND**
- Patient does not have severe hepatic impairment (i.e., total bilirubin >3 times the upper limit of normal); **AND**
- Used as a single agent; **AND**

Acute Myeloid Leukemia (AML) † ‡ Φ [1-5]

- Used as post-remission maintenance treatment; **AND**
  - Patient achieved a complete remission/response (CR) or a complete remission with incomplete blood count recovery (CRi) following intensive induction therapy; **AND**

- Patient is unable to complete intensive curative therapy; **OR**
- Patient is ≥60 years of age and has declined or is not fit/eligible for allogeneic hematopoietic stem cell transplant; **OR**

o Patient has treatment-related disease other than core binding factor and/or unfavorable cytogenetics and/or molecular abnormalities; **AND**

- Patient is <60 years of age and has declined or is not fit/eligible for allogeneic hematopoietic stem cell transplant

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,5,6]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe myelosuppression, etc.; **AND**
- Disease response with treatment as defined by stabilization or improvement as evidenced by a complete response [CR] (i.e., morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

V. Dosage/Administration [1]

Indication	Dose
AML	The recommended dosage of Onureg is 300 mg orally once daily with or without food on Days 1 through 14 of each 28-day cycle. Continue ONUREG until disease progression or unacceptable toxicity.
Note: Due to substantial differences in the pharmacokinetic parameters, the recommended dose and schedule for Onureg are different from those for the IV or SC azacitidine products. Treatment of such patients may not be effective and may result in a fatal adverse reaction. Do not substitute Onureg for intravenous or subcutaneous azacitidine.	

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, not otherwise specified
- C9399 – Unclassified drugs or biologicals *(Hospital Outpatient Use ONLY)*

NDC:

- Onureg 200 mg tablets: 59572-0730-xx

- Onureg 300 mg tablets: 59572-0740-xx

VII. References

1. Onureg [package insert]. Summit, NJ; Celgene, Inc.; May 2021. Accessed July 2021.
2. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) for azacitidine. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
4. Wei A, Dohner H, Pocock C, et al. The QUAZAR AML-001 Maintenance Trial: Results of a Phase III International, Randomized, Double-Blind, Placebo-Controlled Study of CC-486 (Oral Formulation of Azacitidine) in Patients with Acute Myeloid Leukemia (AML) in First Remission. Blood. 2019;134(suppl 2): LBA3. doi:10.1182/blood-2019-132405
5. Roboz GJ, Montesinos P, Selleslag D, et al. Design of the randomized, Phase III, QUAZAR AML Maintenance trial of CC-486 (oral azacitidine) maintenance therapy in acute myeloid leukemia. Future Oncol. 2016 Feb;12(3):293-302. doi: 10.2217/fon.15.326. Epub 2016 Jan 19.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C92.00	Acute myeloblastic leukemia, not having achieved remission
C92.01	Acute myeloblastic leukemia in remission
C92.50	Acute myelomonocytic leukemia, not having achieved remission
C92.51	Acute myelomonocytic leukemia in remission
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.A0	Acute myeloid leukemia with multilineage dysplasia, not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia in remission

ICD-10	ICD-10 Description
C93.00	Acute monoblastic/monocytic leukemia, not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia in remission
C94.00	Acute erythroid leukemia, not having achieved remission
C94.01	Acute erythroid leukemia in remission
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.21	Acute megakaryoblastic leukemia in remission

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC