ONUREG™ (azacitidine) tablets 300 mg • 200 mg

The majority of older patients with acute myeloid leukemia (AML) who achieve remission will relapse[1]

Can you help your patients with AML prolong survival?

An example to guide patients through transitions of care

Indication

ONUREG® is indicated for continued treatment of adult patients with acute myeloid leukemia 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.

Important Safety Information

CONTRAINDICATIONS

ONUREG® is contraindicated in patients with known severe hypersensitivity to azacitidine or its components.

WARNINGS AND PRECAUTIONS

Risks of Substitution with Other Azacitidine Products

Due to substantial differences in the pharmacokinetic parameters, the recommended dose and schedule for ONUREG® are different from those for the intravenous or subcutaneous azacitidine products. Treatment of patients using intravenous or subcutaneous azacitidine at the recommended dosage of ONUREG® may result in a fatal adverse reaction. Treatment with ONUREG® at the doses recommended for intravenous or subcutaneous azacitidine may not be effective. Do not substitute ONUREG® for intravenous or subcutaneous azacitidine.

Myelosuppression

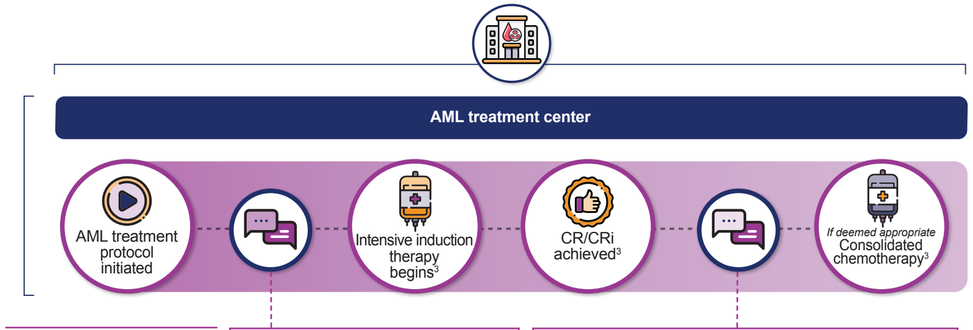
New or worsening Grade 3 or 4 neutropenia and thrombocytopenia occurred in 49% and 22% of patients who received ONUREG®. Febrile neutropenia occurred in 12%. A dose reduction was required for 7% and 2% of patients due to neutropenia and thrombocytopenia. Less than 1% of patients discontinued ONUREG® due to either neutropenia or thrombocytopenia. Monitor complete blood counts and modify the dosage as recommended. Provide standard supportive care, including hematopoietic growth factors, if myelosuppression occurs.

Please see additional Important Safety Information on pages 2-4 and accompanying full Prescribing Information for ONUREG®.

How can you plan for post-remission AML treatment from the start?

Initial patient assessment

- Presents at PCP with symptoms including, but not limited to, fever, bruising, and fatigue[2]
- Additional workup conducted; AML suspected
- Diagnosis confirmed; referred to AML treatment center by local oncologist



Goals of AML treatment plan[4]

1. Achieve remission.
2. Durable disease control.

Critical conversation

Patient/caregiver and oncologist discuss the treatment journey:[5]

- Initial induction to post-remission treatment
- Patient goals

Critical conversation

Patient/caregiver, oncologist, and transplant doctor discuss potential treatment options:[3]

- Consolidation
- HSCT
- Continued treatment with ONUREG® with the opportunity to transition back home

Important Safety Information (cont'd)

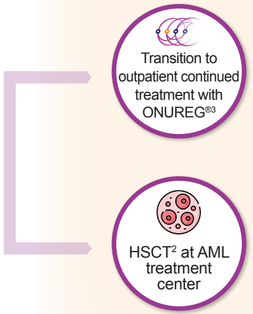
Increased Early Mortality in Patients with Myelodysplastic Syndromes (MDS)

In AZA-MDS-003, 216 patients with red blood cell transfusion-dependent anemia and thrombocytopenia due to MDS were randomized to ONUREG® or placebo. 107 received a median of 5 cycles of ONUREG® 300 mg daily for 21 days of a 28-day cycle. Enrollment was discontinued early due to a higher incidence of early fatal and/or serious adverse reactions in the ONUREG® arm compared with placebo. The most frequent fatal adverse reaction was sepsis. Safety and effectiveness of ONUREG® for MDS have not been established. Treatment of MDS with ONUREG® is not recommended outside of controlled trials.

Embryo-Fetal Toxicity

ONUREG® can cause fetal harm when administered to a pregnant woman. Azacitidine caused fetal death and anomalies in pregnant rats via a single intraperitoneal dose less than the recommended human daily dose of oral azacitidine on a mg/m^2 basis. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 6 months after the last dose.

Abbreviations: AML acute myeloid leukemia; CR, complete remission; CRi, complete remission with incomplete blood count recovery; ER, emergency room; HSCT, hematopoietic stem cell transplantation; PCP, primary care provider.



ONUREG® is indicated by the FDA for continued treatment of adult patients with acute myeloid leukemia 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.[6]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Oral azacitidine (ONUREG®) is a NCCN Category 1, preferred option in the maintenance setting for patients with non-CBF-AML, ≥55 years of age, and who received previous intensive therapy, achieved remission, and for whom no allogeneic HCT is planned, regardless of consolidation status.[7,a,b]

For patients 18 to 54 years of age with non-CBF-AML, oral azacitidine (ONUREG®) is a Category 2A recommended treatment in the maintenance setting, regardless of consolidation status.[a,b]

HSCT may not be an option due to:

- Older age, comorbidities, donor unavailability, worsening performance status, inadequate support, distance from transplant center, patient unwillingness, or risks of treatment[3,8]

[a]This is not intended to replace consolidation chemotherapy. In addition, patients who are fit may benefit from HCT in first CR, and there are no data to suggest that maintenance therapy with oral azacitidine can replace HCT. The panel also notes that the trial did not include patients <55 years of age or those with CBF-AML; it was restricted to patients ≥55 years of age with AML with intermediate or adverse cytogenetics who were not felt to be candidates for HCT. Most patients received at least 1 cycle of consolidation prior to starting oral azacitidine.[9]

[b]The definition of continued and maintenance treatment by the FDA and NCCN differ based on the AML treatment period in patients with or without CR.[7,10]

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Embryo-Fetal Toxicity (cont'd)

Advise males with female partners of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 3 months after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 15% of patients who received ONUREG®. Serious adverse reactions in ≥2% included pneumonia (8%) and febrile neutropenia (7%). One fatal adverse reaction (sepsis) occurred in a patient who received ONUREG®.

Most common (≥10%) adverse reactions with ONUREG® vs placebo were nausea (65%, 24%), vomiting (60%, 10%), diarrhea (50%, 21%), fatigue/asthenia (44%, 25%), constipation (39%, 24%), pneumonia (27%, 17%), abdominal pain (22%, 13%), arthralgia (14%, 10%), decreased appetite (13%, 6%), febrile neutropenia (12%, 8%), dizziness (11%, 9%), pain in extremity (11%, 5%).

Abbreviations: AML, acute myeloid leukemia; CBF, core binding factor; FDA, Food and Drug Administration; HCT, hematopoietic cell transplantation; HSCT, hematopoietic stem cell transplantation, NCCN, National Comprehensive Cancer Network.

Please see additional Important Safety Information on pages 1, 2, and 4 and accompanying full Prescribing Information for ONUREG®.

Potential steps for patients with AML in first remission not proceeding to HSCT

TREATMENT AND SUPPORTIVE CARE	MONITORING	FOLLOW-UP
☐ AML treatment center sends recommendation for continued treatment with ONUREG® to the outpatient care team ☐ 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[6] ☐ Antiemetics should be prescribed for the first 2 cycles of ONUREG®[6] ☐ **Important education for patients:** Antiemetics should be administered 30 minutes prior to each dose of ONUREG®. Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea or vomiting[6] ☐ Physician should review warnings and precautions with ONUREG® ☐ ONUREG® should be continued until disease progression or unacceptable toxicity[6]	☐ CBC monitoring is recommended every other week for the first 2 cycles and prior to the start of each cycle thereafter. Monitoring should be increased to every other week for 2 cycles after any dose reduction for myelosuppression[6] ☐ If ANC is less than 0.5 Gi/L on Day 1 of a cycle, ONUREG® should not be administered. The start of the cycle should be delayed until ANC is 0.5 Gi/L or more[6] ☐ Carefully monitor patients for adverse reactions. If adverse reactions do occur, follow the recommended dosage modifications	☐ Follow-up appointment should be scheduled with the outpatient physician as recommended after ONUREG® initiation ☐ Continue communication between the treatment center and the community center to ensure coordination of care

Important Safety Information (cont'd)

LACTATION

There are no data regarding the presence of azacitidine in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with ONUREG® and for 1 week after the last dose.

Abbreviations: AML, acute myeloid leukemia; ANC, absolute neutrophil count; CBC, complete blood count; CR, complete remission; CRi, complete remission with incomplete blood count recovery; HSCT, hematopoietic stem cell transplantation.

References: 1. Burnett AK. Treatment of acute myeloid leukemia: are we making progress? *Hematology Am Soc Hematol Educ Program*. 2012;2012:16. doi:10.1182/asheducation-2012.1.1 **2.** American Cancer Society. Signs and symptoms of acute myeloid leukemia (AML). Updated February 27, 2024. Accessed March 11, 2024. https://www.cancer.org/cancer/acute-myeloid-leukemia/detection-diagnosis-staging/signs-symptoms.html **3.** American Cancer Society. Typical treatment of acute myeloid leukemia (except APL). Updated July 21, 2023. Accessed March 11, 2024. https://www.cancer.org/cancer/acute-myeloid-leukemia/treating/typical-treatment-of-aml.html **4.** American Cancer Society. Treatment response rates for acute myeloid leukemia (AML). Updated August 21, 2018. Accessed March 11, 2024. https://www.cancer.org/cancer/acute-myeloid-leukemia/treating/response-rates.html **5.** American Cancer Society. Treating acute myeloid leukemia (AML). Accessed March 11, 2024. https://www.cancer.org/cancer/acute-myeloid-leukemia/treating.html **6.** ONUREG (azacitidine). Package insert. Celgene Corp; 2022. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed March 22, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **8.** Lipof JJ, Loh KP, O'Dwyer K, Liesveld JL. Allogeneic hematopoietic cell transplantation for older adults with acute myeloid leukemia. *Cancers (Basel)*. 2018;10(6):179. doi:10.3390/cancers10060179 **9.** Wei AH, Döhner H, Pocock C, et al; QUAZAR AML-001 Trial Investigators. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. *N Engl J Med*. 2020;383(26):2526-2537. doi:10.1056/NEJMoa2004444 **10.** Food and Drug Administration. Acute myeloid leukemia: developing drugs and biological products for treatment. Guidance for industry. FDA website. August 2020. Updated October 17, 2022. Accessed April 4, 2024. https://www.fda.gov/media/162362/download

Please see additional Important Safety Information on pages 1-3 and accompanying full Prescribing Information for ONUREG®.

Bristol Myers Squibb™

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