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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	September 25, 2020
Subject:	Onureg	**Page:**	1 of 5

Last Review Date: December 13, 2024

Onureg

Description

Onureg (azacitidine)

Background

Onureg (azacitidine) is a pyrimidine nucleoside analog of cytidine that inhibits DNA/RNA methyltransferases. Onureg is incorporated into the DNA of cancer cells which inhibits DNA methyltransferases, reduces DNA methylation, and alters gene expression, including re-expression of genes regulating tumor suppression and cell differentiation. Incorporation of Onureg into the RNA of cancer cells inhibits RNA methyltransferases, reduces RNA methylation, decreases RNA stability, and decreases protein synthesis (1).

Regulatory Status

FDA-approved indication: Onureg is a nucleoside metabolic inhibitor indicated for continued treatment of adult patients 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 (1).

Onureg should not be substituted for intravenous or subcutaneous azacitidine. The indications and dosing regimen for Onureg differ from that of intravenous or subcutaneous azacitidine (1).

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. If the absolute neutrophil count (ANC) is less than 0.5 Gi/L on Day 1 of a cycle, do not administer Onureg. Delay the start of the cycle until the ANC is 0.5 Gi/L or more (1).

Myelosuppression including neutropenia and thrombocytopenia may occur with Onureg therapy. Complete blood counts should be monitored 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 the 2 cycles after any dose reduction for myelosuppression (1).

Onureg can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to use effective contraception during treatment with Onureg and for at least 6 months after the last dose. Males with female partners of reproductive potential should be advised to use effective contraception during treatment with Onureg and for at least 3 months after the last dose (1).

The safety and effectiveness of Onureg in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Onureg may be considered **medically necessary** if the conditions indicated below are met.

Onureg may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Acute myeloid leukemia (AML) with **ONE** of the following:
   a. Patient has achieved first complete remission (CR) following intensive induction chemotherapy
   b. Patient has achieved complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy

AND ALL of the following:

1. Patient is not able to complete intensive curative therapy
2. Prescriber agrees to monitor complete blood count (CBC) and absolute neutrophil count (ANC) for myelosuppression and modify the dosage if needed
3. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onureg and for 6 months after the last dose
4. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onureg and for 3 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Acute myeloid leukemia (AML)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor complete blood count (CBC) and absolute neutrophil count (ANC) for myelosuppression and modify the dosage if needed
3. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onureg and for 6 months after the last dose
4. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onureg and for 3 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 42 tablets per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Onureg (azacitidine) is a pyrimidine nucleoside analog of cytidine that inhibits DNA/RNA methyltransferases. Onureg is incorporated into the DNA of cancer cells which inhibits DNA methyltransferases, reduces DNA methylation, and alters gene expression, including re-expression of genes regulating tumor suppression and cell differentiation. Incorporation of Onureg into the RNA of cancer cells inhibits RNA methyltransferases, reduces RNA methylation, decreases RNA stability, and decreases protein synthesis (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Onureg while maintaining optimal therapeutic outcomes.

References

1. Onureg [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; October 2022.
2. NCCN Drugs & Biologics Compendium® Azacitidine 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.

Policy History

Date	Action
September 2020	Addition to PA
December 2020	Annual review
September 2021	Annual review and reference update
September 2022	Annual review and reference update
March 2023	Annual review and reference update
December 2023	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.