HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ONUREG safely and effectively. See full prescribing information for ONUREG.

ONUREG (azacitidine) tablets, for oral use
Initial U.S. Approval: 2004

INDICATIONS AND USAGE

ONUREG is a nucleoside metabolic inhibitor 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 (1).

DOSAGE AND ADMINISTRATION

- **Do not substitute ONUREG for intravenous or subcutaneous azacitidine. The indications and dosing regimen for ONUREG differ from that of intravenous or subcutaneous azacitidine (2.1, 5.1).**
- Administer ONUREG 300 mg orally once daily on Days 1 through 14 of each 28-day cycle (2.2).
- Administer an antiemetic before each dose for at least the first 2 cycles (2.2).

DOSAGE FORMS AND STRENGTHS

Tablets: 200 mg and 300 mg (3).

CONTRAINDICATIONS

History of severe hypersensitivity to azacitidine or its components (4).

WARNINGS AND PRECAUTIONS

- Risks of Substitution with Other Azacitidine Products: Do not substitute ONUREG for intravenous or subcutaneous azacitidine (2.1, 5.1).
- Myelosuppression: Monitor complete blood counts every other week for the first 2 cycles and prior to the start of each cycle thereafter. Increase monitoring to every other week for the 2 cycles after any dose reduction. Withhold and then resume at same or reduced dose or discontinue ONUREG based on severity (2.3, 5.2).
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception (5.4, 8.1, 8.3).

ADVERSE REACTIONS

The most common adverse reactions (≥ 10%) are nausea, vomiting, diarrhea, fatigue/asthenia, constipation, pneumonia, abdominal pain, arthralgia, decreased appetite, febrile neutropenia, dizziness, and pain in extremity.

To report SUSPECTED ADVERSE REACTIONS, contact Celgene Corporation at 1-888-423-5436 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed (8.2).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 9/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Information

Do not substitute ONUREG for intravenous or subcutaneous azacitidine. The indications and dosing regimen for ONUREG differ from that of intravenous or subcutaneous azacitidine *[see Warnings and Precautions (5.1)]*.

2.2 Recommended Dosage

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.

Administer an antiemetic 30 minutes prior to each dose of ONUREG for the first 2 cycles. Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting.

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.

Instruct patients on the following:

- Do not split, crush, or chew ONUREG tablets.
- Take a dose about the same time each day.
- If a dose of ONUREG is missed, or not taken at the usual time, take the dose as soon as possible on the same day, and resume the normal schedule the following day. Do not take 2 doses on the same day.
- If a dose is vomited, do not take another dose on the same day. Resume the normal schedule the following day.

ONUREG is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

2.3 Monitoring and Dosage Modifications for Adverse Reactions

Monitor complete blood count every other week for the first 2 cycles and prior to the start of each cycle thereafter. Increase monitoring to every other week for the 2 cycles after any dose reduction for myelosuppression.

The recommended dosage modifications for adverse reactions are provided in Table 1.

Table 1: Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity	Recommended Dosage Modification
Myelosuppression *[see Warnings and Precautions (5.2)]*	Neutrophils less than 0.5 Gi/L on Cycle Day 1	• Interrupt treatment. Resume at the same dose once neutrophils return to 0.5 Gi/L or higher.
	Neutrophils less than 1 Gi/L with fever at anytime	First Occurrence • Interrupt treatment. Resume at the same dose once neutrophils return to 1 Gi/L or higher. Occurrence in 2 Consecutive Cycles • Interrupt treatment. After neutrophils return to 1 Gi/L or higher, resume at reduced dose of 200 mg. • If a patient continues to experience febrile neutropenia after dose reduction, reduce the treatment duration by 7 days. • If febrile neutropenia reoccurs after dose and schedule reduction, discontinue ONUREG.
	Platelets less than 50 Gi/L with bleeding	First Occurrence • Interrupt dose. Resume at the same dose once platelets return to 50 Gi/L or higher. Occurrence in 2 Consecutive Cycles • Interrupt dose. After platelets return to 50 Gi/L or higher, resume at reduced dose of 200 mg. • If a patient continues to experience thrombocytopenia with bleeding after dose reduction, reduce the treatment duration by 7 days. • If thrombocytopenia with bleeding reoccurs after dose and schedule reduction, discontinue ONUREG.

Adverse Reaction	Severity	Recommended Dosage Modification
Gastrointestinal Toxicity *[see Adverse Reactions (6.1)]*	Grade 3 or 4 Nausea or Vomiting	• Interrupt dose. Resume at the same dose once toxicity has resolved to Grade 1 or lower. • If toxicity reoccurs, interrupt dose until resolved to Grade 1 or lower. Resume at reduced dose of 200 mg. • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days. • If the toxicity continues or reoccurs after dose and schedule reduction, discontinue ONUREG.
	Grade 3 or 4 Diarrhea	• Interrupt dose. Resume at the same dose once toxicity has resolved to Grade 1 or lower. • If toxicity reoccurs, interrupt dose until resolved to Grade 1 or lower. Resume at reduced dose of 200 mg. • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days. • If the toxicity continues or reoccurs after dose and schedule reduction, discontinue ONUREG.
Other Adverse Reactions *[see Adverse Reactions (6.1)]*	Grade 3 or 4	• Interrupt dose and provide medical support. Resume at the same dose once toxicity has resolved to Grade 1 or lower. • If toxicity re-occurs, interrupt dose until resolved to Grade 1 or lower. Resume at reduced dose of 200 mg. • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days. • If the toxicity continues or reoccurs after dose and schedule reduction, discontinue ONUREG.

3 DOSAGE FORMS AND STRENGTHS

Tablets:

- 200 mg, pink, oval, film-coated tablet with debossed “200” on one side and “ONU” on the other side.
- 300 mg, brown, oval, film-coated tablet with debossed “300” on one side and “ONU” on the other side.

4 CONTRAINDICATIONS

ONUREG is contraindicated in patients with known severe hypersensitivity to azacitidine or its components *[see Adverse Reactions (6.2), Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Risks of Substitution with Other Azacitidine Products

Due to substantial differences in the pharmacokinetic parameters *[see Clinical Pharmacology (12.3)]*, 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 of patients using ONUREG at the doses recommended for intravenous or subcutaneous azacitidine may not be effective.

Do not substitute ONUREG for intravenous or subcutaneous azacitidine *[see Dosage and Administration (2.1)]*.

5.2 Myelosuppression

New or worsening Grade 3 or 4 neutropenia and thrombocytopenia occurred in 49% and 22% of patients who received ONUREG, respectively. Febrile neutropenia occurred in 12%. A dose reduction was required for 7% and 2% of patients due to neutropenia and thrombocytopenia, respectively. Less than 1% of patients discontinued ONUREG due to either neutropenia or thrombocytopenia.

Monitor complete blood counts and modify the dosage as recommended *[see Dosage and Administration (2.2, 2.3)]*. Provide standard supportive care, including hematopoietic growth factors, if myelosuppression occurs.

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